Part VI: Summary of the risk management plan

Summary of risk management plan for Lifemin 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg hard capsules

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

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

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

I. The medicine and what it is used for

Lifemin 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.

Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural 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 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.

A comprehensive treatment programme typically includes psychological, educational and social measures as well as pharmacotherapy and is aimed at stabilising children 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 EEG. Learning may or may not be impaired.

Lifemin is not indicated in all children with ADHD and the decision to use this 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 Lifemin should always be used in this way according to the licensed 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 Lifemin, together with measures to minimise such risks and the proposed studies for learning more about Lifemin'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 the case of Lifemin, 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 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 Lifemin is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Lifemin 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 Lifemin. 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

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Important identified risk: Intentional drug misuse, abuse and diversion	
Risk minimisation measures	Routine risk minimisation measures **Covered under the following section of SmPC and PL:** SmPC: Sections 4.2 of SmPC: Patients should be monitored for the risk of diversion, misuse, and abuse

Important identified risk: Intentional drug misuse, abuse and diversion	
	Section 4.4 of SmPC: Consistent with other stimulants, the potential for abuse, misuse or diversion of lisdexamfetamine should be considered prior to prescribing. Advice to patients provided in PL in section 2. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimization measures:** **Educational material:** • Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Carer information – Potential for non-medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None

Important Identified risk: Growth retardation and developmental delay in children and adolescents	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC</u>:** Section 4.2 of SMPC: Growth, height, weight, and appetite should be recorded at least six-monthly with maintenance of a growth chart. Special warnings and precautions for use in Section 4.4 of SmPC on Long-term suppression of growth (height and weight). - Listed as ADRs in Section 4.8 of SmPC.

	Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimization measures:** **Educational material:** • Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapyCarer information – Potential for non-medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None.

Important Identified risk: Psychosis/Mania	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC and PL</u>:** - Special warnings and precautions for use Section 4.4 of SmPC Psychiatric adverse events - Listed as ADRs in Section 4.8 of SmPC. - Listed in PL section 4. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimisation measure(s)** **Educational material:**

Important Identified risk: Psychosis/Mania	
	• Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapyCarer information – Potential for non-medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	None in adults.

Important Identified risk: Hostility/Aggression	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC and PL</u>:** - Contraindication in Section 4.3 of SmPC. - Psychiatric AEs in Section 4.4 of SmPC - Listed as an ADRs in Section 4.8 of SmPC. - Advice to patients provided in PL in section 2. - Listed in PL section 4. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimisation measure(s)** **Educational material:** • Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapyCarer information – Potential for non-

Important Identified risk: Hostility/Aggression	
	medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	None

Important Identified risk: Depression	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC and PL</u>:** Section 4.2 of SmPC: Ongoing monitoring psychiatric should be continually monitored - Section 4.4 of SmPC: Psychiatric adverse events - Listed as an ADRs in Section 4.8 of SmPC. - Advice to patients provided in PL in section 2. Listed in PL section 4. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimisation measure(s)** **Educational material:** • Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapyCarer information – Potential for non-medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	None

Important potential risk: Serious cardiovascular events (including arrhythmias, ischaemic cardiac events, cardiomyopathy, sudden death)	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC and PL</u>:** -Section 4.2 of SmPC: Ongoing monitoring cardiovascular status should be continually monitored - Section 4.4 of SmPC: Cardiovascular adverse events. - Listed as an ADRs in Section 4.8 of SmPC. - Advice to patients provided in PL in section 2. - Listed in PL section 4. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimisation measure(s)** **Educational material:** • Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapyCarer information – Potential for non-medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	None

Important potential risk: Cerebrovascular disorders (ischaemic and haemorrhagic stroke)	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC and PL</u>:** - Section 4.4 of SmPC: Special warnings and precautions for use.

Important potential risk: Cerebrovascular disorders (ischaemic and haemorrhagic stroke)	
	Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimisation measure(s)** **Educational material:** • Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapyCarer information – Potential for non-medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	None

Important potential risk: Syncope	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC</u>:** -Section 4.4 of SmPC: Special warnings and precautions for use. -Listed as ADRs in Section 4.8 of SmPC. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimisation measure(s)** None
Additional pharmacovigilance activities	None

Important potential risk: Suicidality	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC and PL</u>:** -Section 4.4 of SmPC: Special warnings and precautions for use. -Advice to patients provided in PL in section 2. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimisation measure(s)** **Educational material:** • Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapyCarer information – Potential for non-medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	None

Important potential risk: Off-label use	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC</u>:** Risk not presented in Labeling. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None

Important potential risk: Off-label use	
	Additional risk minimisation measure(s) **Educational material:** • Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapyCarer information – Potential for non-medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	None

Important Identified risk: Neonatal effects on growth (via lactation)	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC</u>:** - Section 4.6 of SmPC: Fertility, pregnancy and breast-feeding - Advice to patients provided in PL in section 2. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimization measures:** None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None.

Missing information: Safety in pregnant women	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC and PL</u>:**

Missing information: Safety in pregnant women	
	- Section 4.6 of SmPC: Fertility, pregnancy and breast-feeding - Advice to patients provided in PL in section 2. Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems. **Other routine risk minimisation measures** None **Additional risk minimisation measure(s)** **Educational material:** • Chart for the ongoing monitoring of lisdexamfetamine dimesylate therapy • Prescriber Checklist 1: Lisdexamfetamine dimesylate checklist before prescribing • Prescriber Checklist 2: Checklist for the ongoing monitoring of lisdexamfetamine dimesylate therapyCarer information – Potential for non-medical use and diversion of prescription stimulant medications
Additional pharmacovigilance activities	None

Important potential risk: Safety in the elderly	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC</u>:** - Section 4.2 of SmPC: Posology and method of administration Prescription only medicine Legal status: Prescription should be initiated and supervised by physicians experienced in the management of MS (restricted medical prescription in EU). **Other routine risk minimisation measures** None **Additional risk minimisation measure(s)** None

Important potential risk: Safety in the elderly	
Additional pharmacovigilance activities	None

Important potential risk: Long-term safety (cardiovascular and cerebrovascular effects) in adults	
Risk minimisation measures	Routine risk minimisation measures **<u>Covered under the following section of SmPC</u>:** - Section 4.2 of SmPC: Posology and method of administration Prescription only medicine Legal status: It is prescribed only by doctors who have experience in treating people with behaviour problems **Other routine risk minimisation measures** None
Additional pharmacovigilance activities	None

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 authorization or specific obligation of Lifemin.

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

There are no studies required for Lifemin.