Summary of risk management plan for Dexamfetamine Sulfate

This is a summary of the risk management plan (RMP) for Dexamfetamine Sulfate 5 mg Tablets (dexamfetamine sulfate). The RMP details important risks of dexamfetamine sulfate, how these risks can be minimised, and how more information will be obtained about dexamfetamine sulfate's risks and uncertainties (missing information).

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

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

I. The medicine and what it is used for

Dexamfetamine sulfate is authorised for comprehensive treatment programme for attentiondeficit/hyperactivity disorder (ADHD) in children and adolescents aged 6 to 17 years when response to previous methylphenidate treatment is considered clinically inadequate (see SmPC for the full indication). It contains dexamfetamine sulfate as the active substance and it is given by oral route of administration.

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

Important risks of dexamfetamine sulfate, together with measures to minimise such risks and the proposed studies for learning more about dexamfetamine sulfate'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 dexamfetamine sulfate, 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, including PSUR assessment 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 dexamfetamine sulfate is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of dexamfetamine sulfate 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 dexamfetamine sulfate. 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);

Summary of safety concerns	
Important identified risks	• Drug abuse and dependency • Misuse and diversion • Withdrawal syndrome • Psychotic reactions e.g. hallucination (visual, auditory, skin sensation), and mania • Increased risk of depression • Increased risk of aggressive/hostile behaviour • Cardiac and cardiovascular disorders, including increased blood pressure versus hypertension and increased heart rate, tachycardia, arrhythmias • Cardiomyopathy • Decreased rate of growth and development/anorexia • Serious skin reaction
Important potential risks	• Ischaemic/serious cardiovascular events e.g. myocardial infarction, sudden death, cyanosis, QT prolongation • Cerebrovascular disorders e.g. stroke (ischaemic and haemorrhagic) • Migraine • Raynaud's syndrome • Suicidal ideation • Tics/Tourette's/dystonias • Repetitive behaviours • Seizures • Delayed sexual maturation and neonatal growth • Neonatal toxicity, e.g. cardio-respiratory toxicity • Carcinogenicity • Overdose • Off-label use

Missing information	• Long-term safety (cardiovascular, growth, neurological, cognition and psychotic) • Pregnancy • Patients with renal and hepatic insufficiency • Treatment in children under 6 years, adults and elderly

II.B Summary of important risks

Important identified risk - Drug abuse and dependency	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Pharmacist information letter Parent/carer information Letter
Important identified risk - Misuse and diversion	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3 and 4.4. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Pharmacist information letter Parent/carer information Letter
Important identified risk - Withdrawal syndrome	

Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4, 4.6 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Considerations on dexamfetamine sulfate cessation
Important identified risk - Psychotic reactions e.g. hallucination (visual, auditory, skin sensation), and mania	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8. Pack of 28 tablets. Additional risk minimisation measures:

Important identified risk - Drug abuse and dependency	
	Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter Chart for ongoing patient monitoring
Important identified risk - Increased risk of depression	

Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter Chart for ongoing patient monitoring
Important identified risk - Increased risk of aggressive/hostile behaviour	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter Chart for ongoing patient monitoring
Important identified risk - Cardiac and cardiovascular disorders, including increased blood pressure versus hypertension and increased heart rate, tachycardia, arrhythmias	
Risk minimisation measures	Routine risk minimisation measures:

Important identified risk - Drug abuse and dependency

	SmPC section 4.3, 4.4, 4.5 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter Chart for ongoing patient monitoring
Important identified risk - Cardiomyopathy	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter Chart for ongoing patient monitoring
Important identified risk - Decreased rate of growth and development/anorexia	

Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter Chart for ongoing patient monitoring
Important identified risk - Serious skin reaction	

Important identified risk - Drug abuse and dependency	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: None
Important potential risk - Ischaemic/serious cardiovascular events e.g. myocardial infarction, sudden death, cyanosis, QT prolongation	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4, 4.5 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter Chart for ongoing patient monitoring

Important potential risk - Cerebrovascular disorders e.g. stroke (ischaemic and haemorrhagic)	
Risk minimisation measures SmPC section 4.3, 4.4, 4.5	Routine risk minimisation measures: and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter
Important potential risk - Migraine	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.8. Pack of 28 tablets.

Important identified risk - Drug abuse and dependency	
	Additional risk minimisation measures: None
Important potential risk - Raynaud's syndrome	
Routine risk minimisation	measures: SmPC section 4.8. Pack of 28 tablets. Additional risk minimisation measures: None
Important potential risk - Suicidal ideation	

Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter Chart for ongoing patient monitoring
Important potential risk - Tics/Tourette's/dystonias	
Risk minimisation measures SmPC section 4.3, 4.4, 4.5	Routine risk minimisation measures: and 4.8. Pack of 28 tablets. Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Prescriber Checklist (2) for monitoring of ongoing therapy Considerations on dexamfetamine sulfate cessation Pharmacist information letter
Important potential risk - Repetitive behaviours	
Risk minimisation measures	Routine risk minimisation measures:

Important identified risk - Drug abuse and dependency	
	SmPC section 4.3, 4.4 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: None
Important potential risk - Seizures	

Risk minimisation measures SmPC section 4.4 and 4.8.	Routine risk minimisation measures: Pack of 28 tablets. Additional risk minimisation measures: None
Important potential risk - Delayed sexual maturation and neonatal growth	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4, 4.6, 4.8 and 5.3. Pack of 28 tablets. Additional risk minimisation measures: None
Important potential risk - Neonatal toxicity, e.g. cardio-respiratory toxicity	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.6 and 5.3. Pack of 28 tablets. Additional risk minimisation measures: None
Important potential risk - Carcinogenicity	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 5.3 Pack of 28 tablets. Additional risk minimisation measures: None
Important potential risk - Overdose	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.2, 4.5 and 4.9.

Important identified risk - Drug abuse and dependency	
	Pack of 28 tablets. Additional risk minimisation measures: None

Important potential risk - Off-label use	
Risk minimisation measures Pack of 28 tablets.	Routine risk minimisation measures: Additional risk minimisation measures: Physician information letter Prescriber Checklist (1) prior to the initiation of treatment Pharmacist information letter
Missing Information - Long-term safety (cardiovascular, growth, neurological, cognition and psychotic)	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4. Pack of 28 tablets. Additional risk minimisation measures: None
Missing Information - Pregnancy	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.6 and 5.3. Pack of 28 tablets. Additional risk minimisation measures: None
Missing Information - Patients with renal and hepatic insufficiency	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.8. Pack of 28 tablets. Additional risk minimisation measures: None
Missing Information - Treatment in children under 6 years, adults and elderly	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.2, 4.4 and 4.8.
Important identified risk - Drug abuse and dependency	

	Pack of 28 tablets. Additional risk minimisation measures: None

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 dexamfetamine sulfate.

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

There are no studies required for dexamfetamine sulfate.