Part VI: Summary of the risk management plan

Summary of risk management plan for DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets

This is a summary of the risk management plan (RMP) for **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets**.

The RMP details important risks of **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets** and how more information will be obtained about risks of **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets** and uncertainties (missing information).

The summary of product characteristics (SmPC) and package leaflet of **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets** give essential information to healthcare professionals and patients on how **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets** should be used.

I. The medicine and what it is used for

DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets is authorised for the treatment of attention deficit hyperactivity disorder (ADHD).

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

Important risks of **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets**, together with measures to minimise such risks and the proposed studies for learning more about the risks of **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets**, are outlined below.

Measures to minimise the risks identified for **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets** are:

• Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

- Educational tool for physicians;
- Letters to patients, parents and caregivers;
- Specific questionnaire.

• The medicine's legal status — The medicinal product is supplied to the patient as "prescription only" medicine.

Together, these measures constitute routine risk minimisation measures.

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 LAROPHARM 5/10/20 mg tablets** is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets** are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 LAROPHARM 5/10/20 mg tablets**. 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 longterm use of the medicine).

Important identified risks	1. Drug abuse and dependency 2. Misuse and diversion 3. Cardiac and cardiovascular disorders, including increased blood pressure versus hypertension and increased heart rate, tachycardia, arrhythmias 4. Cardiomyopathy 5. Increased risk of depression 6. Increased risk of aggressive / hostile behavior 7. Psychotic reactions, e.g. hallucination (visual, auditory, skin sensation), and mania 8. Withdrawal syndrome 9. Decreased rate of growth and development / anorexia 10. Serious skin reaction
Important potential rsks	1. Ischaemic / serious cardiovascular events, e.g. myocardial infarction, sudden death, cyanosis, QT prolongation 2. Cerebrovascular disorders, e.g. stroke (ischaemic and haemorrhagic) 3. Migraine 4. Raynaud's syndrome 5. Suicidal ideation 6. Tics / Tourette's / dystonias 7. Repetitive behaviours 8. Seizures 9. Delayed sexual maturation and neonatal growth 10. Neonatal toxicity, e.g. cardio-respiratory toxicity

	11. Carcinogenicity 12. Overdose 13. Off-label use
Missing information	1. Long-term safety (cardiovascular, growth, neurological, cognition and psychotic) 2. Pregnancy 3. Patients with renal and hepatic insufficiency 4. Treatment in children under 6 years, adults, and elderly

II.B Summary of important risks

1. Drug abuse and dependency	
Evidence for linking the risk to the medicine	Literature; Approved Product Information (Summary of Product Information = SPC) for oral sodium bicarbonate products; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016); Carvalho M, Carmo H, Costa VM, Capela JP, Pontes H, Remião F, Carvalho F, Bastos Mde L. Toxicity of amphetamines: an update. Arch Toxicol. 2012 Aug;86(8):1167-231. doi: 10.1007/s00204-012-0815-5. Epub 2012 Mar 6. Review. PMID: 22392347.
Risk factors and risk groups	Patients with history of drug abuse and/or dependence
Risk minimisation measures	Prescription only medicine Routine Pharmarovigilance measures: appropriate information in SmPCs: section 4.3, section 4.4, section 4.8. Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and

	checklists) letter to pharmacists, parents and caregivers specific questionnaire.
2. Misuse and diversion	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients with dexamphetamine prescriptions
Risk minimisation measures	Routine Pharmacovigilance measures: appropriate information in SmPCs: section 4.4. prescription only medicine. Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and checklists) letter to pharmacists, parents and caregivers specific questionnaire.
3. Cardiac and cardiovascular disorders, including increased blood pressure versus hypertension and increased heart rate, tachycardia, arrhythmias	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Generally, ADHD drugs should not be used in patients with known structural cardiac abnormalities. Before prescribing an ADHD drug, it is important to be aware of whether the patient has: • a family history of sudden death, or death related to cardiac problems; • participates in strenuous exercise; or

	• takes other sympathomimetic drugs These are thought to be additional risk factors. In patients with relevant risk factors, and based on the physician's judgment, further evaluation of the cardiovascular system may be considered before starting on the drug. American Heart Association recommends that before beginning therapy of stimulant medications, careful history should be obtained with special attention to symptoms, such as palpitations, syncope, or near syncope. Medications use, such as other prescribed and over-the-counter medications, should be determined. The family history should be reviewed with reference to the long QT Syndrome or other causes of sudden, unexplained death. Detection of these symptoms, or risk factors, warrants a cardiovascular evaluation by a pediatric cardiologist before initiation of therapy.
Risk minimisation measures	SmPCs: section 4.3, section 4.4, section 4.5, section 4.8. prescription only medicine Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and checklists)
5. Cardiomyopathy	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients with renal and/or cardiac disorders
Risk minimisation measures	SmPCs: section 4.3, section 4.4, section 4.5, section 4.8. prescription only medicine Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and

	checklists)
5. Increased risk of depression	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: section 4.3, section 4.4, section 4.8. prescription only medicine Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and checklists)
6. Increased risk of aggressive / hostile behavior	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: section 4.3, section 4.4, section 4.8. prescription only medicine Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and checklists) specific questionnaire
7. Psychotic reactions, e.g. hallucination (visual, auditory, skin sensation), and mania	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: section 4.3, section 4.4, section 4.8. prescription only medicine Additional Pharmacovigilance measures:

	educational tool (physician's guide to prescribing and checklists) specific questionnaire
8. **Withdrawal syndrome**	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients who stop taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: section 4.4, section 4.8. prescription only medicine Additional Pharmacovigilance measures: none
9. **Decreased rate of growth and development / anorexia**	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: section 4.3, section 4.4, section 4.8. prescription only medicine Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and checklists) specific questionnaire
10. Serious skin reaction	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: section 4.8. prescription only medicine Additional Pharmacovigilance measures: none

Summary of important potential risks

1. Ischaemic / serious cardiovascular events, e.g. myocardial infarction, sudden death, cyanosis, QT prolongation	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: sections 4.3, 4.4, 4.5 and 4.8. Prescription only medicine Additional Pharmacovigilance measures: Educational tool (physician's guide to prescribing and checklists) Specific questionnaire
2. Cerebrovascular disorders, e.g. stroke (ischaemic and haemorrhagic)	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: sections 4.3, 4.4, 4.5 and 4.8. Prescription only medicine Additional Pharmacovigilance measures: Educational tool (physician's guide to prescribing and checklists) Specific questionnaire
3. Migraine	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.

Risk minimisation measures	SmPCs: sections 4.4 and 4.8. prescription only medicine Additional Pharmacovigilance measures: none
4. Raynaud's syndrome	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	Prescription only medicine Additional Pharmacovigilance measures: none
5. Suicidal ideation	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: sections 4.3, 4.4, and 4.8. prescription only medicine Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and checklists)
6. Tics / Tourette's / dystonias	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: sections 4.3, 4.4, 4.5 and 4.8. prescription only medicine Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and checklists)

7. Repetitive behaviours	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: sections 4.4, 4.8. prescription only medicine Additional Pharmacovigilance measures: none
8. Seizures	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: section 4.4. prescription only medicine Additional Pharmacovigilance measures: none
9. Delayed sexual maturation and neonatal growth	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: section 4.6, 5.3. prescription only medicine Additional Pharmacovigilance measures: none
10. **Neonatal toxicity, e.g. cardio-respiratory toxicity**	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: sections 4.6, 5.3.

	prescription only medicine Additional Pharmacovigilance measures: none
11. Carcinogenicity	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: section 5.3. prescription only medicine Additional Pharmacovigilance measures: none
12. Overdose	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: sections 4.1, 4.2., 4.9. prescription only medicine Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and checklists)
13. Off-label use	
Evidence for linking the risk to the medicine	Literature; approved SPC; List of safety concerns along with the risk minimisation measures proposed, submitted for **Amfexa** (MEDICE Arzneimittel Pütter GmbH & Co. KG) was approved (version 5.0 dated 22.01.2016).
Risk factors and risk groups	Patients taking dexamphetamine sulphate.
Risk minimisation measures	SmPCs: sections 4.1, 4.2. prescription only medicine Additional Pharmacovigilance measures: educational tool (physician's guide to prescribing and checklists)

	letter to pharmacists, parents and carers

Missing information

1. Long-term safety (cardiovascular, growth, neurological, cognition and psychotic)	
Risk minimisation measures	SmPCs: section 4.6, section 5.3 prescription only medicine Additional Pharmacovigilance: **educational tool (physician's guide to prescribing and checklists for ongoing monitoring)**
2. Pregnancy	
Risk minimisation measures	SmPCs: section 4.6 prescription only medicine Additional Pharmacovigilance: none
3. Patients with renal and hepatic insufficiency	
Risk minimisation measures	SmPCs: section 4.2, section 4.4 prescription only medicine Additional Pharmacovigilance: none
4. **Treatment in children under 6 years, adults, and elderly**	
Risk minimisation measures	SmPCs: section 4.1, section 4.2 Additional Pharmacovigilance: 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 LAROPHARM 5/10/20 mg tablets.**

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

There are no studies required for **DEXAMFETAMINE LAROPHARM 5/10/20 mg tablets.**