Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for METHYLPHENIDATE HYDROCHLORIDE

This is a summary of the risk management plan (RMP) for METHYLPHENIDATE HYDROCHLORIDE prolonged release tablets 18, 27, 36, 54 mg and modified-release hard capsules 10, 20, 30, 40 and 60 mg (hereinafter referred to as Methylphenidate hydrochloride). The RMP details important risks of Methylphenidate hydrochloride, how these risks can be minimised, and how more information will be obtained about Methylphenidate hydrochloride's risks and uncertainties (missing information).

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

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

I. The Medicine and What It is used for

Methylphenidate hydrochloride is authorised for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 6 years of age and above as part of a comprehensive treatment programme (see SmPC for the full indication). It contains methylphenidate as the active substance and it is given orally.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

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

II.A List of Important Risks and Missing Information

Important risks of Methylphenidate hydrochloride 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 Methylphenidate hydrochloride. 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 7: Summary of Safety Concerns

List of important risks and missing information	
Important identified risks	• Hypertension • Tachycardia • Raynaud's phenomenon • Hallucinations (auditory, skin, sensation, visual disturbance) • Psychosis/Mania • Anorexia • Decreased rate of growth • Aggression • Depression • Damage to the liver caused by medication • Priapism
Important potential risks	• Cardiomyopathy • Migraine • Repetitive behaviours • QT prolongation • Cyanosis • Arrhythmias

	• Sudden death • Ischaemic cardiac events • Cerebrovascular disorders • Hostility • Suicidality • Tics/Tourette's syndrome/Dystonias • Effect on final height • Sexual maturation (delayed) • Carcinogenicity • Off-label use • Diversion • Withdrawal syndrome • Drug abuse and Drug dependence • Lymphocytic leukaemia • Neonatal cardio-respiratory toxicity neonatal/foetal tachycardia, respiratory distress/apnoea) • Neonatal effects on growth
Missing information	• Long-term cardiovascular effects • Long-term cerebrovascular effects • Long-term psychiatric effects

II.B Summary of Important Risks

Table 8: Summary of Risk Minimisation Activities by Safety Concern

Safety concern	**Risk minimisation measures**
Important identified risks	
Hypertension	**Routine risk minimisation measures:** Mentioned in contraindications in SmPC section 4.3. Risk is listed in SmPC section 4.8. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Tachycardia	**Routine risk minimisation measures:** Risk is listed in SmPC section 4.8.

Safety concern	Risk minimisation measures
	Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Hallucinations (auditory, skin, sensation, visual disturbance)	**Routine risk minimisation measures:** Recommendation for discontinuation of treatment in case a possible causal role for has been identified for methylphenidate is included in SmPC sections 4.4. Emergence of new psychotic or manic symptoms is discussed in section in SmPC section 4.4. Risk is listed in SmPC section 4.8. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Psychosis/Mania	**Routine risk minimisation measures:** Contraindications listed in SmPC section 4.3. Psychiatric disorders are described in SmPC section 4.4. Risk is listed in SmPC section 4.8. Recommendation for monitoring in case of development or worsening of psychiatric disorders is included in SmPC section 4.4. Recommendation for discontinuation of treatment in case a possible causal role for has been identified for methylphenidate is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Anorexia	**Routine risk minimisation measures:** Contraindications listed in SmPC section 4.3. Risk is listed in SmPC section 4.8. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Decreased rate of growth	**Routine risk minimisation measures:** Reduced weight gain and growth retardation are described in SmPC section 4.4. Risk is listed in SmPC section 4.8. Recommendations for pre-treatment screening and ongoing monitoring using a growth chart are included in SmPC sections 4.2. Prescription only medicine. **Additional risk minimisation measures:**

Safety concern	Risk minimisation measures
	Educational tool for HCPs.
Aggression	**Routine risk minimisation measures:** Aggressive or hostile behaviour are described in SmPC section 4.4. Recommendation monitoring of psychiatric disorders, including aggressive or hostile behaviour is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Depression	**Routine risk minimisation measures:** Contraindications listed in SmPC section 4.3. Recommendation monitoring of psychiatric disorders, including depression is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Important potential risks	
Cardiomyopathy	**Routine risk minimisation measures:** Pre-existing cardiovascular disorders, including cardiomyopathies are stated as contraindication in SmPC section 4.3. Pre-treatment screening and ongoing monitoring recommendations with regards to cardiovascular status are stated in SmPC section 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Arrhythmias	**Routine risk minimisation measures:** Risk of arrhythmia is listed in SmPC section 4.8. Recommendation for cardiovascular status monitoring is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Sudden death	**Routine risk minimisation measures:** Discussed in SmPC section 4.4. Recommendation for cardiovascular status monitoring is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.

Safety concern	Risk minimisation measures
Ischaemic cardiac events	**Routine risk minimisation measures:** Risk is listed in SmPC section 4.8. Recommendation for cardiovascular status monitoring is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Cerebrovascular disorders	**Routine risk minimisation measures:** Pre-existing cerebrovascular disorders are a contraindication stated in SmPC section 4.3. Discussed in SmPC section 4.4. Risk is listed in SmPC section 4.8. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Hostility	**Routine risk minimisation measures:** Aggressive or hostile behaviour are described in SmPC section 4.4. Recommendation monitoring of psychiatric disorders, including aggressive or hostile behaviour is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Suicidality	**Routine risk minimisation measures:** Suicidal tendencies are a contraindication listed in SmPC section 4.3. Discussed in SmPC section 4.4. Risk is listed in SmPC section 4.8. Recommendation on monitoring of psychiatric disorders is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Tics/Tourette's syndrome/Dystonias	**Routine risk minimisation measures:** Discussed in SmPC section 4.4. Risk is listed in SmPC section 4.8. Recommendation on monitoring of psychiatric disorders is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:**

Safety concern	Risk minimisation measures
	Educational tool for HCPs.
Off-label use	**Routine risk minimisation measures:** Instructions and recommendations that methylphenidate should always be used in this way according to the licensed indication and according to prescribing/diagnostic guidelines listed in SmPC section 4.2. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Diversion	**Routine risk minimisation measures:** Abuse, misuse and diversion are discussed in SmPC section 4.4. Recommendations on monitoring for the risk of diversion, misuse and abuse of methylphenidate are listed in SmPC section 4.2. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Withdrawal syndrome	**Routine risk minimisation measures:** Risk is discussed in SmPC section 4.4. Recommendation on monitoring of patients on long-term therapy is included in SmPC sections 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Drug abuse and Drug dependence	**Routine risk minimisation measures:** Abuse, misuse and diversion are discussed in SmPC section 4.4. Risk is listed in SmPC section 4.8. Recommendations on monitoring for the risk of diversion, misuse and abuse of methylphenidate are listed in SmPC section 4.2. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.
Missing information	
Long-term cardiovascular effects	**Routine risk minimisation measures:** Long-term use in children and adolescents is discussed in SmPC section 4.2. Consequences and unknown information regarding long-term use are discussed throughout SmPC section 4.4. Dose reduction and discontinuation recommendation in SmPC section 4.2. Monitoring recommendations regarding long-term use in SmPC
Long-term cerebrovascular effects	
Long-term psychiatric effects	

Safety concern	Risk minimisation measures
	section 4.4. Prescription only medicine. **Additional risk minimisation measures:** Educational tool for HCPs.

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 Methylphenidate hydrochloride.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Methylphenidate hydrochloride.