PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for methylphenidate

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

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

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

I. The medicine and what it is used for

Methylphenidate is authorised for Attention Deficit / Hyperactivity Disorder (ADHD) in children aged 6 years of age and over and adolescents when remedial measures alone prove insufficient. It contains methylphenidate as the active substance and it is taken once daily in the morning.

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

Important risks of methylphenidate, together with measures to minimise such 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 public (e.g. with or without prescription) can help to minimises its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse events is collected continuously and is regularly analysed, including in 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 methylphenidate is not yet available, it is listed under 'missing information' below.

In the case of methylphenidate, the routine measures described above are supplemented with additional risk minimisation measures, mentioned under relevant risks below.

II.A List of important risks and missing information

Important risks of methylphenidate are those risks that need special risk management activities to further investigate or minimise them, so that the medicinal product can be safely taken by patients. 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. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but the definite causal 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/use in special patient populations etc.);

Table 6 Part VI: Summary of safety concerns

List of important risks and missing information	
Important identified risks	High blood pressure (Hypertension) Fast heart beat (Tachycardia) Fingers and toes feeling numb, tingling and changing colour (from white to blue, then red) when cold (Raynaud's phenomenon) Seeing, feeling, or hearing things that are not real [Hallucinations (auditory, skin sensation, visual disturbance)] Believing things that are not true or a break from reality/feeling unusually excited, overactive, and uninhibited (Psychosis/Mania) Loss of appetite or decreased appetite (Anorexia) Feeling aggressive (Aggression) Feeling depressed (Depression) Lack of weight gain or height growth (Decreased rate of growth)

List of important risks and missing information	
	Abnormal persistent erection of the penis (Priapism)
Important potential risks	Disorder of the heart's electrical system that predisposes individuals to irregular heartbeats, fainting spells, and sudden death (QT prolongation) Skin and mucous membranes turn blue or purple (Cyanosis) Problem with the rate or rhythm of the heartbeat (Arrhythmias) Sudden death Effects when heart muscle does not get enough oxygen (Ischaemic cardiac events) Severe headache felt as a throbbing pain at the front or side of the head (Migraine) Effects on the blood vessels or blood supply of the brain (Cerebrovascular disorders) Repetitive behaviours Hostility Thinking about or feeling like killing yourself, suicidal attempt (Suicidality) Hard-to-control, repeated twitching of any parts of the body or repeating sounds and words/uncontrolled speech and body movements/involuntary muscle contractions causing uncontrollable movements (Tics/Tourette's syndrome/Dystonias) Effect on final height Sexual maturation (delayed) Carcinogenicity Lymphocytic leukaemia

List of important risks and missing information	
	Use of methylphenidate other than for an approved use (Off-label use) Transfer of methylphenidate from a legal to an illegal channel of distribution or use (Diversion) Drug abuse and Drug dependence Side effects when treatment is stopped (Withdrawal syndrome) Neonatal cardio-respiratory toxicity (neonatal/foetal tachycardia, respiratory distress/apnoea) Neonatal effects on growth (via lactation) Disease of the heart muscle (Cardiomyopathy)
Missing information	Long-term safety

II.B Summary of important risks

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

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.

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

There are no studies required for methylphenidate.