PART VI SUMMARY OF THE RISK MANAGEMENT PLAN

SUMMARY OF RISK MANAGEMENT PLAN FOR STRIVERDI RESPIMAT (OLODATEROL HYDROCHLORIDE)

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

Striverdi Respimat's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Striverdi Respimat should be used.

This summary of the RMP for Striverdi Respimat should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of which are part of the European Public Assessment Report (EPAR).

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

I. THE MEDICINE AND WHAT IT IS USED FOR

Striverdi Respimat is authorised for once daily maintenance bronchodilator treatment in patients with chronic obstructive pulmonary disease (COPD). It contains olodaterol hydrochloride as the active substance and it is given by oral inhalation via a propellant-free metered dose inhaler called the Respimat Soft Mist Inhaler.

Further information about the evaluation of Striverdi Respimat's benefits can be found in Striverdi Respimat's EPAR, including in its plain-language summary, available on the European Medicines Agency website, under the medicine's webpage.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Striverdi Respimat, together with measures to minimise such risks and the proposed studies for learning more about Striverdi Respimat'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 as 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.

If important information that may affect the safe use of Striverdi Respimat is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Striverdi Respimat 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 Striverdi Respimat. 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 yet been established 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).

PVI.Table 1 Summary table of the safety concerns

Important identified risks	None
Important potential risks	Cardiac arrhythmia Myocardial ischaemia
Important missing information	Long-term data beyond 1 year of use (adverse cardiovascular outcome) Patients with a recent history of: - myocardial infarction - unstable or life-threatening cardiac arrhythmia - paroxysmal tachycardia - decompensated heart failure Safety in pregnant or breast-feeding women

II.B Summary of important risks

Summaries of the important risks and missing information for Striverdi Respimat are provided in the following tables.

PVI.Table 2 Cardiac arrhythmia

Important potential risk of cardiac arrhythmia	
Evidence for linking the risk to the medicine	General occurrence of cardiac arrhythmia was low in the olodaterol long-term trials. Olodaterol 5 mcg and 10 mcg-treated patients showed cardiac arrhythmia frequencies of 5.6% and 4.4%, respectively, vs 4.2% and 4.3% in the placebo and active comparator groups. In the post-marketing setting, 18 cases have been reported, 1 of which associated with a fatal outcome.
Risk factors and risk groups	Tobacco smoking, obesity, hyperlipdaemia, sedentary life style, diabetes and hypertension are major risk factors for ischaemic (coronary) heart disease. Ischaemic heart disease and previous myocardial infarction, together with pulmonary heart disease and congestive heart failure, are the most prominent physiological risk factors for cardiac arrhythmia. Pharmacological risk factors are the co-administration of pulmonary medications with pro-arrhythmic effects such as xanthines, beta-adrenergic agonists or anticholinergics.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 advises use with caution in patients with a history of cardiovascular disorders or in case of a planned operation with halogenated hydrocarbon anaesthetic. SmPC Section 4.8 advises that undesirable effects related to the beta-adrenergic agonist class be taken into consideration. Prescription-only medicine. Additional risk minimisation measures: None.
Additional pharmacovigilance activities	Cohort study 1222.54.

PVI.Table 3 Myocardial ischaemia

Important potential risk of myocardial ischaemia	
Evidence for linking the risk to the medicine	General occurrence of myocardial ischaemia symptoms was low in the olodaterol long-term trials. Olodaterol 5 mcg and 10 mcg-treated patients showed myocardial ischaemia frequencies of 1.1% and 1.6%, respectively, vs 1.7% and 0.7% in the placebo and active comparator groups. In the post-marketing setting, 4 cases have been reported, 1 of which associated with a fatal outcome.
Risk factors and risk groups	Major risk factors are current smoking or history of smoking, chronic hypertension, hyperlipidaemia, obesity, sedentary lifestyle and diabetes leading to coronary heart disease.

PVI.Table 3 (cont'd) Myocardial ischaemia

Important potential risk of myocardial ischaemia (cont'd)	
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 advises use with caution in patients with a history of cardiovascular disorders. SmPC Section 4.8 advises that undesirable effects related to the beta-adrenergic agonist class be taken into consideration. Prescription-only medicine. Additional risk minimisation measures: None.
Additional pharmacovigilance activities	Cohort study 1222.54.

PVI.Table 4 Long-term data beyond 1 year of use (adverse cardiovascular outcome)

Missing information of long-term data beyond 1 year of use (adverse cardiovascular outcome)	
Risk minimisation measures	Routine risk minimisation measures: Prescription-only medicine. Additional risk minimisation measures: None.
Additional pharmacovigilance activities	Cohort study 1222.54.

PVI.Table 5 Patients with a recent history of myocardial infarction, unstable or life-threatening cardiac arrhythmia, paroxysmal tachycardia, decompensated heart failure

Missing information of patients with a recent history of myocardial infarction, unstable or life-threatening cardiac arrhythmia, paroxysmal tachycardia, decompensated heart failure	
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 advises use with caution in these patient groups. Prescription-only medicine. Additional risk minimisation measures: None.
Additional pharmacovigilance activities	Cohort study 1222.54.

PVI.Table 6 Safety in pregnant or breast-feeding women

Missing information of safety in pregnant or breast-feeding women	
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.6 states that it is preferable to avoid use during pregnancy. SmPC Section 4.6 states that a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from therapy. Prescription-only medicine. Additional 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 for the marketing authorisation or specific obligation for Striverdi Respimat.

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

Study 1222.54: Cohort study of cardiovascular events in patients with chronic obstructive pulmonary disease initiating olodaterol or other long-acting beta$_2$ agonists.

Purpose of the study: This BI-sponsored, non-interventional PASS was planned as RMP commitment suggested by the Medicines Evaluation Board from the Netherlands. The study aims to obtain further information on the risk of selected cardiac arrhythmias, acute myocardial infarction and other serious ischaemic heart disease events, including unstable angina, in patients with COPD exposed to olodaterol compared with the risk in patients exposed to other long-acting beta$_2$-agonists (LABAs). Further information on the risk of overall mortality in patients with COPD exposed to olodaterol compared with the risk in patients exposed to other LABAs will also be collected.

ABBREVIATIONS

BI	Boehringer Ingelheim
COPD	Chronic obstructive pulmonary disease
EPAR	European Public Assessment Report
LABA	Long-acting beta$_2$-agonist
PASS	Post-Authorisation Safety Study

RMP	Risk Management Plan
SmPC	Summary of Product Characteristics