Summary of risk management plan for ROLUFTA ELLIPTA

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

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

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

Important new concerns or changes to the current ones will be included in updates of ROLUFTA ELLIPTA's RMP.[i]

I. The medicine and what it is used for

ROLUFTA ELLIPTA is authorised for maintenance bronchodilator treatment to relieve symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD) (see SmPC for the full indication). It contains umeclidinium bromide as the active substance and it is given by inhalation route.

Further information about the evaluation of ROLUFTA ELLIPTA's benefits can be found in ROLUFTA ELLIPTA's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage: link to product's EPAR summary landing page on the EMA webpage.

https://www.ema.europa.eu/en/medicines/human/EPAR/rolufta-ellipta

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

Important risks of ROLUFTA ELLIPTA, together with measures to minimise such risks and the proposed studies for learning more about [invented name]'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 ROLUFTA ELLIPTA, these measures are supplemented with *additional risk minimization 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 ROLUFTA ELLIPTA is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of ROLUFTA ELLIPTA 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 ROLUFTA ELLIPTA. 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);

List of important risks and missing information	
Important identified risks	None
Important potential risks	Cardio- and Cerebrovascular Disorders
	Lower Respiratory Tract Infection (incl. pneumonia)
Missing information	None

II.B Summary of important risks

Important potential risk: Cardio- and cerebrovascular disorders	
Evidence for linking the risk to the medicine	Cardiovascular effects have been associated with use of long-acting muscarinic antagonists in patients with COPD, however, no clear associations have been observed in the clinical development programme for UMEC.
Risk factors and risk groups	Patients with severe cardiovascular disease are at increased risk of future cardiovascular events. Older age, a history of previous cardiac disease and worse lung function were predictive of increased risk of cardiovascular events in the COPD population [**Error! Reference source not found.**, 2007].
Risk minimisation measures	**Routine risk minimisation measures**: Section 4.4 and section 4.8 of the SmPC (also Section 2 and 4 of Product Leaflet). **Additional risk minimisation measures**: None.
Additional pharmacovigilance activities	**Additional pharmacovigilance activities**: Study 201038,Post-authorisation Safety (PAS) Observational Cohort Study to Quantify the Incidence and Comparative Safety of Selected Cardiovascular and Cerebrovascular Events in COPD Patients Using Inhaled UMEC/VI Combination, or Inhaled UMEC versus Tiotropium.. *See section II.C of this summary for an overview of the post-authorisation development plan.*

Important potential risk: Lower Respiratory Tract Infection (incl. pneumonia)	
Evidence for linking the risk to the medicine	The risk of pneumonia is associated with use of long-acting muscarinic antagonists in patients with COPD, no associations have been observed in the clinical development programme for UMEC
Risk factors and risk groups	The incidence of pneumonia, including pneumonia requiring hospitalisation, in a COPD population is dependent upon several patient characteristics, such as increasing age, COPD severity, low BMI (<20), male gender, concurrent smoking, and the presence of co-morbid conditions [**Error! Reference source not found.**, 2009].

Important potential risk: Lower Respiratory Tract Infection (incl. pneumonia)	
Risk minimisation measures	**Routine risk minimisation measures**: Section 4.8 of the SmPC (also Section 2 and 4 of Product Leaflet). **Additional risk minimisation measures**: None.
Additional pharmacovigilance activities	**Additional pharmacovigilance activities**: None

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

The following studies are conditions of the marketing authorisation:

Study Short Name: Post-authorisation Safety (PAS) Observational Cohort Study to Quantify the Incidence and Comparative Safety of Selected Cardiovascular and Cerebrovascular Events in COPD Patients Using Inhaled UMEC/VI Combination, or Inhaled UMEC versus Tiotropium (Study201038).

Purpose of the Study: The purpose of this study is to expand understanding of the potential cardiovascular (CV) and cerebrovascular risks of myocardial infarction (MI), stroke and new onset or acute worsening/decompensation heart failure of UMEC/VI and UMEC as compared to tiotropium. Tiotropium is a LAMA with a well-established safety and efficacy profile.

The primary objectives of the study are:

1. To demonstrate non-inferiority of UMEC/VI combination and UMEC to tiotropium for risk of the composite endpoint of MI, stroke, heart failure or sudden cardiac death based on an analysis of time to first event for new users of UMEC/VI combination, UMEC or Tiotropium.

2. To quantify the incidence rate and frequency of the composite endpoint of MI, stroke, heart failure or sudden cardiac death for new users of UMEC/VI combination, UMEC, and tiotropium.