Summary of risk management plan for Trelegy Ellipta

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

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

This summary of the RMP for Trelegy 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 Trelegy Ellipta RMP.

I. The medicine and what it is used for

Trelegy Ellipta is indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) for relief of symptoms and reduction in exacerbations. It contains FF/UMEC/VI as the active substance and it is given by oral inhalation only.

Further information about the evaluation of Trelegy Ellipta's benefits will be found in Trelegy Ellipta's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

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

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

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

II.A List of important risks and missing information

Important risks of Trelegy Ellipta 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 Trelegy 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);

Summary of safety concerns	
Important identified risks	Pneumonia
Important potential risks	Serious Cardiovascular Events
Missing information	None

II.B Summary of important risks

Important Identified Risk: Pneumonia	
Evidence for linking the risk to the medicine	In the Article 31 review (17 March 2016) conducted by Pharmacovigilance Risk Assessment Committee (PRAC) evaluating indirect comparisons of the risk of pneumonia in COPD patients treated with ICS, it was concluded that COPD patients treated with ICS are at increased risk of pneumonia, however, there was no conclusive evidence of differences in this risk for different products CTT116855 was a large phase III study of over 10.000 patients where 4,151 patients were treated with FF/UMEC/VI, 4,134 with FF/VI and 2,070 with UMEC/VI for 52 weeks. There was a higher incidence of any event in the pneumonia AESI group in FF/UMEC/VI (317 subjects [8%]) and FF/VI (292 subjects [7%]) groups compared with the UMEC/VI group (97 subjects [5%]) Given the higher incidence of pneumonia in the FF containing arms, and the class risk of pneumonia with ICS use in patients with COPD, and the conclusion of the PRAC review, pneumonia is considered an important identified risk with FF/UMEC/VI.
Risk factors and risk groups	The following risk factors in COPD have been identified: a prior history of pneumonia (as opposed to no prior history), BMI <25 kg/m2, reduced FEV1 (i.e. FEV1 <50% predicted) and inhaled corticosteroids use.
Risk minimisation measures	**Routine risk minimisation measures**: Section 4.4 and section 4.8 of the SmPC (also Section 4 of Product Leaflet). **Additional risk minimisation measures**: None

Important potential risk: Serious cardiovascular events	
Evidence for linking the risk to the medicine	Cardiovascular effects have been associated with use of muscarinic antagonists and β_2-agonists in patients with COPD, however, no clear associations have been observed in the clinical development programme for FF/UMEC/VI.
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.
Risk minimisation measures	**Routine risk minimisation measures**: Section 4.4 and section 4.8 of the SmPC (also Section 4 of Product Leaflet). **Additional risk minimisation measures**: 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 Trelegy Ellipta.

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

There are no studies required for Trelegy Ellipta.