

## **PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN**

### **VI.1 Summary of risk management plan for Temybric Ellipta**

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

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

This summary of the RMP for Temybric 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 Temybric Ellipta RMP.

### **VI.2 The medicine and what it is used for**

Temybric 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 Temybric Ellipta's benefits will be found in Temybric 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/temybric-ellipta>

### **VI.3 Risks associated with the medicine and activities to minimise or further characterise the risks**

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

### VI.3.1 List of important risks and missing information

Important risks of Temybric 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 Temybric 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);

<b>Summary of safety concerns</b>	
Important identified risks	Pneumonia
Important potential risks	Serious Cardiovascular Events
	Decreased bone mineral density and associated fractures
Missing information	None

### VI.3.2 Summary of important risks

<b>Important Identified Risk: Pneumonia</b>	
Evidence for linking the risk to the medicine	<p>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</p> <p>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%])</p> <p>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.</p>
Risk factors and risk groups	Following risk factors have been identified: a prior history of pneumonia (as opposed to no prior history), BMI <25 kg/m <sup>2</sup> , reduced FEV <sub>1</sub> (i.e. FEV <sub>1</sub> <50% predicted) and inhaled corticosteroids use.
Risk minimisation measures	<p><b>Routine risk minimisation measures:</b></p> <p>Section 4.4 and section 4.8 of the SmPC (also Section 4 of Product Leaflet).</p> <p><b>Additional risk minimisation measures:</b> None</p>

<b>Important potential risk: Serious cardiovascular events</b>	
Evidence for linking the risk to the medicine	Cardiovascular effects have been associated with use of muscarinic antagonists and $\beta_2$ -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	<p>Patients with severe cardiovascular disease are at increased risk of future cardiovascular events.</p> <p>Older age, a history of previous cardiac disease and worse lung function were predictive of increased risk of cardiovascular events in the COPD population.</p>
Risk minimisation measures	<p><b>Routine risk minimisation measures:</b></p> <p>Section 4.4 and section 4.8 of the SmPC (also Section 4 of Product Leaflet).</p> <p><b>Additional risk minimisation measures:</b> None</p>

<b>Important potential risk: Decreased Bone Mineral Density and Associated Fractures</b>	
Evidence for linking the risk to the medicine	Decreased bone mineral density (BMD) and associated fractures have been associated with use of corticosteroids in patients with COPD, however, no clear association has been observed in the clinical development programme for FF/UMEC/VI. However, these effects are usually only anticipated at exposure levels much higher than those expected with ICS. Therefore, the risk of decreased BMD and associated fracture is potential for the exposure dosage.
Risk factors and risk groups	Prolonged immobilization, family history of osteoporosis, post-menopausal status, tobacco use, advanced age, poor nutrition, or chronic use of drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids).
Risk minimisation measures	<b>Routine risk minimisation measures:</b> Section 4.4 and section 4.8 of the SmPC (also Section 4 of Product Leaflet). <b>Additional risk minimisation measures:</b> None

## **VI.4 Post-authorisation development plan**

### **VI.4.1 Studies which are conditions of the marketing authorisation**

There are no studies which are conditions of the marketing authorisation or specific obligation of Temybric Ellipta.

### **VI.4.2 Other studies in post-authorisation development plan**

There are no studies required for Temybric Ellipta.

Medicinal product no longer authorised