EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 September 2024
EMA/565794/2024
Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): umeclidinium bromide

Procedure No. EMEA/H/C/PSR/S/0048

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Scientific conclusions

Taking into account the PRAC Assessment Report for the non-interventional imposed PASS final study report for the medicinal products mentioned above, the scientific conclusions of CHMP are as follows:

Rolufta Ellipta, Incruse Ellipta, Anoro Ellipta and Laventair Ellipta (umeclidinium bromide, umeclidinium bromide/vilanterol) are removed from the additional monitoring list as the condition to the marketing authorisation has been fulfilled. This relates to the conduction of a Post-authorisation Safety Observational Cohort Study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events (MI, stroke, heart failure or sudden cardiac death) in COPD patients using inhaled UMEC/VI combination or inhaled UMEC versus Tiotropium (Study 201038) which was imposed as a condition to the Marketing Authorisation (category 1 PASS), due to concerns on cardiovascular and cerebrovascular safety. According to the protocol, the HR (95% CI) were calculated for each treatment comparison; the non-inferiority criterion was the upper bound of the 95% confidence interval (CI) around the hazard ratio not exceeding 2.0 and the lower bound of the 95% CI not exceeding 1.0. Other secondary safety endpoints were studied. Effectiveness outcomes were also evaluated, such as persistence with study medication, frequency of exacerbations.

The adjusted HR (95% CI) for the composite outcome was 1.254 (0.830, 1.896) for UMEC vs. TIO cohorts, and 1.352 (0.952, 1.922) for UMEC/VI vs. TIO. The adjusted HR of UMEC/VI vs TIO is not statistically significant, but close to the established limits. An increased risk of MI was observed in UMEC/VI cohort with respect to tiotropium: adjusted HR of 2.195 (1.053, 4.575). The risk of MI was lower between the UMEC and TIO (adjusted HR (95% CI) of 1.754 (0.748, 4.115)). It is acknowledged that the study was powered to test for differences between cohorts for the primary composite endpoint only and not to test for non-inferiority in the secondary endpoints; however, such difference in the MI risk is to be noted.

COPD, Pneumonia and Lower respiratory tract infection were the most frequently reported events in patients who had received UMEC/VI for longer than one year. The majority of the serious events were attributed to exacerbation complicating advanced stage COPD in most of the cases; excluding a potential relationship with the treatment UMEC/VI.

In conclusion, the PRAC considered that the benefit-risk balance of the concerned medicinal products remained unchanged.

This PASS study was a condition of the marketing authorisations of medicinal products containing the active substance umeclidinium bromide, umeclidinium bromide/vilanterol. This condition is now considered fulfilled and consequently an update of the Annex II conditions or restrictions with regard to the safe and effective use of the medicinal product is recommended to remove this condition as well as deletion of additional monitoring statements in Annexes I and IIIB.

Having reviewed the PRAC recommendation, the CHMP agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for umeclidinium bromide, umeclidinium bromide / vilanterol the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing umeclidinium bromide, umeclidinium bromide / vilanterol is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.