EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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): lumacaftor / ivacaftor

Procedure No. EMEA/H/C/PSUSA/00010455/201705

Period covered by the PSUR: 20 Nov 16 to 19 May 2017

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## Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for lumacaftor/ivacaftor, the scientific conclusions of CHMP are as follows:

In the pooled Phase 3 studies there was a higher incidence of AEs of blood creatine phosphokinase (CPK) increased in subjects who received the approved LUM/IVA dose regimen compared to the placebo group (7.3% versus 5.4%). Furthermore the 2 serious AEs of blood CPK increased and 4 discontinuations all occurred in subjects receiving the approved LUM/IVA dosage regimen. By contrast there were no serious AEs of blood CPK increased, or discontinuations in the placebo group.

To date there have been 48 post-marketing cases that reported AEs associated with increased CPK in patients taking Orkambi, accounting for 0.5% of the total post-marketing reports for Orkambi. Within the total 48 reports, 17 events were considered serious and 31 non-serious. A number of the cases (9/48) may be considered confounded for various reasons but the role of LUM/IVA in contributing to the event in these cases cannot be excluded. Additionally there have been 6 cases where causality is considered possible involving a positive dechallenge, 4 of these 6 cases included a subsequent positive rechallenge. Therefore, PRAC recommends an update of section 4.8 of the SmPC to add 'Blood creatine phosphokinase increased' with frequency 'common'.

The CHMP agrees with the scientific conclusions made by the PRAC.

## Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for lumacaftor/ivacaftor the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing lumacaftor/ivacaftor 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.