22 May 2025
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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): ivacaftor / tezacaftor / elexacaftor

Procedure No. EMEA/H/C/PSUSA/00010868/202410

Period covered by the PSUR: 21 April 2024 to 20 October 2024

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## Scientific conclusions

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

In view of available data on elevated transaminases and hepatic injury from spontaneous reports including in 2 cases a close temporal relationship and in view of a plausible mechanism of action, the PRAC considers a causal relationship between ivacaftor / tezacaftor / elexacaftor and drug induced liver injury is at least a reasonable possibility. The PRAC concluded that the product information of products containing ivacaftor / tezacaftor / elexacaftor should be amended accordingly.

In view of available data on insomnia, anxiety and behavioural changes from the literature and spontaneous reports including in some cases a close temporal relationship, a positive re-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between ivacaftor / tezacaftor / elexacaftor and insomnia, anxiety and behavioural changes is at least a reasonable possibility. The PRAC concluded that the product information of products containing ivacaftor / tezacaftor / elexacaftor should be amended accordingly.

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 ivacaftor / tezacaftor / elexacaftor the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing ivacaftor / tezacaftor / elexacaftor 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.