12 October 2023
EMA/580796/2023
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): tezacaftor / ivacaftor

Procedure No. EMEA/H/C/PSUSA/00010730/202302

Period covered by the PSUR: 12/02/2022 To: 11/02/2023

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

© European Medicines Agency, 2023. Reproduction is authorised provided the source is acknowledged.

Scientific conclusions

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

In view of available data on risk of occurrence of depression and related events from spontaneous reports in post-marketing surveillance, including in some cases a close temporal relationship and a positive de-challenge and re-challenge, and in the context of updates made to the product information for ELX/TEZ/IVA, the PRAC considered that a causal relationship between IVA/TEZ and depression is at least a reasonable possibility.

In addition, the PRAC recommends an update to the product information to reflect that tezacaftor, ivacaftor is excreted in human breastmilk based on data from 2 publications which demonstrated excretion of both actives in the breastmilk of 5 patients. As such, the MAH is requested to update section 4.6 wording relating to breastfeeding.

The PRAC requests the MAH to provide a cumulative review of all data related to excretion in breast milk including available literature evidence wat the next PSUR for Symkevi. Furthermore, the same cumulative review including all available data and literature) should also be provided for the upcoming PSUR for Kaftrio (DLP 20 October 2023).

The PRAC also recommended that the product information of medicinal products containing IVA/TEZ/ELX should be amended accordingly at the next regulatory opportunity.

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