15 December 2022
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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): tafamidis

Procedure No. EMEA/H/C/PSUSA/00002842/202205

Period covered by the PSUR: 16 May 2021 To: 15 May 2022

**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

## Scientific conclusions

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

The adverse event of "Diarrhoea" is listed with a "very common" frequency in section 4.8 of the SmPC of Vyndaqel 20 mg, and disproportionality has been found with PT "Diarrhoea" and tafamidis in EudraVigilance. Furthermore, in view of available data on cases of diarrhoea from spontaneous reports and clinical trial data, including a temporal relationship in 3 cases with high dosage of tafamidis (61 mg or 80 mg), and in view of the seriousness of one case (diarrhoea leading to renal insufficiency and death), the PRAC concluded that the product information of **Vyndaqel 61 mg** should be amended accordingly.

In view of available data on cases of rash and pruritus from spontaneous reports and clinical trial data, including in 19 cases a close temporal relationship, in 4/19 cases a positive dechallenge and in 1/19 cases a positive rechallenge, the PRAC considers that the causal relationship between high dosage of tafamidis and the events of rash or pruritus is at least a reasonable possibility. In 3/19 cases, these cutaneous events occurred when tafamidis doses were increased from 20 mg/day to 61 mg/day or 80 mg/day. Most of these reported cases (17/19) concerned high dosage of tafamidis (61 mg or 80 mg); 10/19 concerned tafamidis 61 mg. Given these data, the PRAC concluded that the product information of **Vyndaqel 61 mg** should be amended accordingly.

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