

Annex IV

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

Scientific conclusions

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

- In view of available data on the risk of “necrotizing fasciitis of the perineum (Fournier’s gangrene)” from the literature and spontaneous reports of Fournier’s gangrene reported in non-diabetic population and in view of a plausible mechanism of action, the PRAC considers that there is sufficient evidence to justify an amendment of the product information in order to indicate that this ADR can occur irrespective of the indication. The PRAC concluded that the product information of products containing empagliflozin should be amended accordingly.
- In view of the available data on phimosis from spontaneous reports and the plausible mechanism of action, PRAC considers there is sufficient evidence to justify an amendment of the product information to highlight that genital infections may result in phimosis that can require circumcision. The PRAC concluded that the product information of products containing empagliflozin should be amended accordingly.
- In view of the available data on haematocrit increased/polycythaemia from the literature and spontaneous reports and the plausible mechanism of action, the PRAC considers there is sufficient evidence to justify an amendment of section 4.4 of the SmPC to reflect that patients with pronounced elevations in haematocrit should be monitored and investigated for underlying haematological disease. The PRAC concluded that the product information of products containing empagliflozin should be amended accordingly.
- In view of the available data on prolonged ketoacidosis and prolonged glucosuria from the literature and spontaneous reports, the PRAC considers there is sufficient evidence to justify an amendment of section 4.4 of the SmPC related to the warning on ketoacidosis to indicate that ketoacidosis may be prolonged after discontinuation of empagliflozin in some patients. The PRAC concluded that the product information of products containing empagliflozin 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 empagliflozin, empagliflozin/metformin the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing empagliflozin, empagliflozin/metformin 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.