

Annex I

**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 testosterone (topical use), the scientific conclusions are as follows:

In view of available literature data on the risk of increase in haemoglobin and haematocrit levels due to interaction with sodium-glucose co-transporter 2 (SGLT-2) inhibitors, the PRAC considers a causal relationship between testosterone and SGLT-2 inhibitors at least a reasonable possibility. The PRAC concluded that the product information of products containing testosterone (topical use) should be amended accordingly.

In view of available literature data on secondary exposure of pets to transdermal hormone-containing medicines, the PRAC concludes that the current guidance for the user to prevent accidental transfer to others, should be extended to also include pets. The PRAC concluded that the product information of products containing testosterone (topical use) should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh 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 testosterone (topical use) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing testosterone (topical use) is unchanged subject to the proposed changes to the product information.

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

Annex II

Amendments to the product information of the nationally authorised medicinal product(s)

Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike-through~~)

Summary of Product Characteristics

- Section 4.2

Following administration

[...]

Patients should be advised to wear clothing that covers the application site at all times to prevent accidental transfer to other **persons as well as pets.**

- Section 4.5

An interaction should be added as follows:

Insulin and other anti-diabetic medicines:

Androgens may improve glucose tolerance and decrease the need for insulin or other anti-diabetic medicines in diabetic patients (see section 4.4). Patients with diabetes mellitus should therefore be monitored especially at the beginning or end of treatment and at periodic intervals during (name of the product) treatment.

Concomitant use of testosterone replacement therapy and sodium-glucose co-transporter 2 (SGLT-2) inhibitors has been associated with an increased risk of erythrocytosis. Since both substances may independently elevate haematocrit levels, a cumulative effect is possible (see also section 4.4). Monitoring of haematocrit and haemoglobin levels is recommended in patients receiving both treatments.

Package Leaflet

- Section 2: What you need to know before you use {(Invented) name}

Other medicines and {(Invented) name}

Tell your doctor ...

- medicines used to treat diabetes. It may be necessary to adjust the dose of your blood sugar reducing medicine. Like other androgens, testosterone may increase the effect of insulin. **Taking SGLT-2 inhibitors (such as empagliflozin, dapagliflozin or canagliflozin) together with testosterone may increase the number of red blood cells in your blood. Your doctor may need to monitor your blood more regularly.**

- Section 3: How to use {(Invented) name}

Similar or stricter wording that is already implemented may be kept.

After applying {(Invented) name}

- [...]
- Wear clothing that covers the application site at all times to prevent accidental transfer to other **persons as well as pets.**