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 (all formulations apart from topical use), the scientific conclusions are as follows:

Based on the review of literature and in particular the data from the Glueck et al (2017, 2018) studies, the PRAC considers that the existing warning regarding clotting disorders should be amended by adding the need of caution in patients with VTE risk factors, adding a warning that in thrombophilic patients, VTE cases have been reported even under anticoagulation treatment and recommending careful evaluation of continuous testosterone treatment after first thrombotic event in these patients. Moreover, the PRAC considers necessary to include the VTE risk factors in the Package Leaflet to highlight this information to patients.

The CMDh 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 testosterone (all formulations apart from topical use) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing testosterone (all formulations apart from topical use) is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing testosterone (all formulations apart from topical use) are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

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 4.4

Clotting disorders

Testosterone should be used with caution in patients with thrombophilia **or risk factors for venous thromboembolism (VTE)**, as there have been post-marketing studies and reports of thrombotic events **(e.g. deep-vein thrombosis, pulmonary embolism, ocular thrombosis)** in these patients during testosterone therapy. **In thrombophilic patients, VTE cases have been reported even under anticoagulation treatment, therefore continuing testosterone treatment after first thrombotic event should be carefully evaluated. In case of treatment continuation, further measures should be taken to minimise the individual VTE risk.**

Package Leaflet

2. What you need to know before you are given [product name]

Warnings and precautions

Talk to your doctor before using [product name] if you have or have ever had:

[…]

- blood clotting problems

- […]
- thrombophilia (an abnormality of blood coagulation that increases the risk of thrombosis - blood clots in blood vessels)
- **factors that increase your risk for blood clots in a vein: previous blood clots in a vein; smoking; obesity; cancer; immobility; if one of your immediate family has had a blood clot in the leg, lung or other organ at a young age (e.g. below the age of about 50); or as you get older.**

  How to recognise a blood clot: painful swelling of one leg or sudden change in colour of the skin e.g. turning pale, red or blue, sudden breathlessness, sudden unexplained cough which may bring up blood; or sudden chest pain, severe light headedness or dizziness, severe pain in your stomach, sudden loss of vision. Seek urgent medical attention if you experience one of these symptoms.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	September 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	3 November 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	2 January 2020