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:

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 (all formulations apart from topical use) should be amended accordingly.

In view of available data from spontaneous reports on the risk of pulmonary oil microembolism (POME), the PRAC considers a causal relationship between testosterone (all formulations apart from topical use) and POME at least a reasonable possibility. The PRAC concluded that the product information of products containing testosterone (all formulations apart from 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 (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 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
Similar or stricter wording that is already implemented may be kept.

- Section 4.4

A warning should be added as follows:

As with all oily solutions, (name of the product) must be injected strictly intramuscularly and very slowly. Pulmonary microembolism of oily solutions can in rare cases lead to signs and symptoms such as cough, dyspnoea, malaise, hyperhydrosis, chest pain, dizziness, paraesthesia, or syncope. These reactions may occur during or immediately after the injection and are reversible. The patient should therefore be observed during and immediately after each injection in order to allow for early recognition of possible signs and symptoms of pulmonary oily microembolism. Treatment is usually supportive, e.g. by administration of supplemental oxygen.

- 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.

- Section 4.8

The following adverse reaction should be added under the SOC “Respiratory, thoracic and mediastinal disorders” with a frequency ’rare’:

Pulmonary oil microembolism

The following text should be added under subsection “Description of selected adverse reactions”:

Pulmonary microembolism of oily solutions can in rare cases lead to signs and symptoms such as cough, dyspnoea, malaise, hyperhydrosis, chest pain, dizziness, paresthesia, or syncope. These reactions may occur during or immediately after the injections and are reversible.

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 4: Possible side effects

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

Rare side effects (may affect up to 1 in 1000 patients):

The oily liquid (name of the product) may reach the lungs (pulmonary microembolism of oily solutions) which can in rare cases lead to signs and symptoms such as cough, shortness of breath, feeling generally unwell, excessive sweating, chest pain, dizziness, "pins and needles", or fainting. These reactions may occur during or immediately after the injection and are reversible. The patient should therefore be observed during and immediately after each injection in order to allow for early recognition of possible signs and symptoms of pulmonary oily microembolism.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	18 September 2025
Transmission to National Competent Authorities of the translations of the annexes to the position:	2 November 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	1 January 2026