

Testosterone-containing medicinal products – Caution in patients with thrombophilia or risk factors for venous thromboembolism (VTE)

Following a recent periodic review of oral, topical, and injectable testosterone-containing medicinal products*, the European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) has recommended an update to the product information for testosterone-containing medicinal products. These products are licensed in Ireland as testosterone replacement therapy for male hypogonadism. Based on a review of the literature, and in particular data from studies by Glueck et al.^{1,2}, the PRAC considered that the existing warning in the product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)) regarding clotting disorders should be amended to highlight the need for caution in patients with risk factors for venous thromboembolism (VTE). Similarly, a warning will be included to indicate that in patients with thrombophilia, cases of VTE have been reported, including some in those on anticoagulant treatment. Therefore, continuing testosterone treatment after a first thrombotic event in patients with thrombophilia should be carefully evaluated, and in the case of treatment continuation, further measures should be taken to minimise the individual VTE risk. Moreover, the PRAC considered it pertinent to specify risk factors for VTE in the Package Leaflet and additionally to include signs and symptoms of thrombosis in order to highlight these for patients.

Advice to Healthcare Professionals

- Topical, oral and injectable testosterone-containing medicinal products should be used with caution in patients with risk factors for venous thromboembolism (VTE).
- In patients with thrombophilia, cases of VTE have been reported, including some in those on anticoagulant treatment. Continuing testosterone treatment in patients with thrombophilia requires careful evaluation after a first thrombotic event and implementation of measures to minimise the individual VTE risk.

Key Message

- Topical, oral and injectable testosterone-containing medicinal products should be used with caution in patients with risk factors for venous thromboembolism (VTE).
- In patients with thrombophilia, cases of VTE have been reported, including some in those on anticoagulant treatment, and continuing testosterone treatment in such patients requires careful evaluation after a first thrombotic event.
- The product information for testosterone-containing medicinal products are being updated to reflect the outcome of the PRAC review.
- All reports of suspected adverse reactions should be reported to the HPRA via the available methods (www.hpra.ie/report).

**Testosterone-containing medicines licensed in Ireland include Androgel, Nebido, Restandol Testocaps, Testarzon, Testim, Testogel, and Tostran. Further details on testosterone-containing medicines are available at www.hpra.ie and www.ema.europa.eu.*

References

- 1) Glueck CJ, Goldenberg N, Wang P. Thromboembolism peaking 3 months after starting testosterone therapy: testosterone-thrombophilia interactions. *J Investig Med.* 2018;66:733-738.
- 2) Glueck CJ, Goldenberg N, Wang P. Testosterone Therapy, Thrombophilia, Venous Thromboembolism, and Thrombotic Events. *J Clin Med.* 2018;8(1).