PRAC review does not confirm increase in heart problems with Testosterone medicines

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Information on Testosterone®

Testosterone is a natural hormone, known as an androgen, found in men and women. In men with hypogonadism, testosterone levels are abnormally low affecting normal sexual development. In Malta the following products are authorised and are prescription-only medicines;

Active Ingredients	Product Name	Authorisation Number
Testosterone 100mg	Testosterone Implant 100mg	AA045/00701
Testosterone Enantate 250mg	Testosterone Enantate Ampoules	AA707/00501
Testosterone 50mg/5g	Testim 50mg Gel	MA832/00901
Testosterone undecanoate 250mg/ml	Nebido	MA 185/02701

Information from the European Medicines Agency about the safety concern

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has completed an EU-wide review of testosterone-containing medicines following concerns over serious side effects on the heart and blood vessels, including heart attack (see MA circular **P12/2014** for more information).

The PRAC review did not find consistent evidence that the use of testosterone in men who do not produce enough testosterone (a condition known as hypogonadism) increases the risk of heart problems. The committee considered that the benefits of testosterone continue to outweigh its risks but recommended that testosterone-containing medicines should only be used where lack of testosterone has been confirmed by signs and symptoms as well as laboratory tests.

The evidence about the risks of serious side effects on the heart of these medicines is inconsistent. While some studies including three recently published studies[1] [2,3] did suggest an increased risk of heart problems in men using testosterone compared with men not taking it, these studies had some limitations and others did not confirm this risk. [4,5] The PRAC also noted that the lack of testosterone itself could increase the risk of heart problems. The PRAC therefore recommended that testosterone-containing medicines should only be used if the lack of testosterone has been confirmed by signs and symptoms as well as laboratory tests. The EU product information for all testosterone-containing medicines should be updated to include this recommendation as well as warnings against use in men suffering from severe heart, liver or kidney problems. The limited data on safety and effectiveness in patients over 65 years of age as well as the fact

[1] Xu et al. 2013
[2] Vigen et al. "Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels" JAMA. 2013 Nov 6;310 (17):1829-1836.
[3] Finkle et al. "Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men." PLoS One. 2014 Jan 29;9(1):e85805.
[4] Baillargeon J, Urban RJ, Kuo Y-F, Ottenbacher KJ, Raji MA, Du F, Lin Y-I, Goodwin JS. Risk of myocardial infarction in older men receiving testosterone therapy. Ann Pharmacother 2014; 48(9):1138-1144.
[5] Corona G, Maseroli E, Rastrelli G, Isidori A, Mannucci E, Maggi M. Cardiovascular risk associated with testosterone boosting medications: a systematic review and metaanalysis. Exp Opin Drug Safety 2014 (Posted online on August 19, 2014. (doi:10.1517/14740338.2014.950653)

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that testosterone levels decrease with age and that age-specific testosterone reference values do not exist will be highlighted in the product information.

The safety of testosterone medicines should continue to be monitored. In particular, a number of studies are still ongoing and their results will be considered in future regular benefit-risk assessments for these medicines.

For more information on testosterone please visit **www.ema.europa.eu**

The PRAC recommendation will now be forwarded to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) which will adopt a final position.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on testosterone containing medicines. Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Prof. John J Borg PhD (Bristol)
Post-licensing Director

Healthcare professionals and patients are encouraged to regularly check the Medicine Authority website for product safety updates as these are issued on an ongoing basis.

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