



NATIONAL PBM BULLETIN

February 7, 2014

DEPARTMENT OF VETERANS AFFAIRS VETERANS HEALTH ADMINISTRATION (VHA)
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),
AND CENTER FOR MEDICATION SAFETY (VA MEDSAFE)

TESTOSTERONE PRODUCTS AND CARDIOVASCULAR SAFETY

I. ISSUE

Two recent studies identify a possible risk of increased cardiovascular events in men receiving testosterone therapy. FDA continues to evaluate this association between testosterone treatment and increased risk of stroke, heart attack, or death, but has not yet reached a firm conclusion.¹

II. BACKGROUND

Testosterone use is indicated for men with testosterone deficiency associated with a medical condition, such as genetic problems, chemotherapy, or other biochemical disorders affecting the production of testosterone by the testicles. Low testosterone levels in the absence of a medical condition are not an approved indication for testosterone products. FDA-approved testosterone formulations consist of a topical gel, transdermal patch, buccal system (applied to upper gum or inner cheek), and injection.

III. DISCUSSION

Two publications have prompted FDA to reassess the cardiovascular safety of testosterone therapy. One observational study looking at elderly men in the U.S. Veteran Affairs health system who underwent coronary angiography to assess for coronary artery disease and had a low serum testosterone suggested a 30 percent increase in risk for stroke, heart attack, and death in the group that received testosterone therapy compared to the group that did not receive any testosterone therapy. Many of these patients had underlying cardiovascular disease.² Another observational study reported an increased risk of heart attack in older men (two-fold increase in the risk of heart attack among men aged 65 years and older within 90 days after initial prescription), as well as in younger men with pre-existing heart disease (a two- to three-fold increase in the risk of heart attack within 90 days after initial prescription). Younger men with no history of heart disease who received a prescription for testosterone did not demonstrate an increased risk of heart attack.³

IV. PROVIDER RECOMMENDATIONS

FDA recommends that:

- Providers should consider whether the benefits of FDA-approved testosterone treatment will outweigh the potential risks of treatment.
- Providers should comply with the prescribing information in the product labelling.
- Patients should not discontinue their testosterone treatment without prior discussion with their health care providers.

Providers should continue to report any adverse reactions with the use of testosterone products by entering the information into CPRS' Allergies/ Adverse Reactions field and/or via local reporting mechanisms. Adverse events should also be reported, as appropriate, to the VA ADERS program and FDA MedWatch (1-800-FDA-1088, fax 1-800-FDA-0178, online at <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>, or by mail).

V. REFERENCES

1. FDA Drug Safety Communication. FDA evaluating risk of stroke, heart attack and death with FDA-approved testosterone products. <http://www.fda.gov/Drugs/DrugSafety/ucm383904.htm> . Accessed 01/31/2014.
2. Vigen R, O'Donnell CI, Baron AE, et al. Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels. JAMA. 2013;310(17):1829-1836.
3. Finkle WD, Greenland S, Ridgeway GK, Adams JL, Frasco MA, et al. (2014) Increased Risk of Non-Fatal Myocardial Infarction Following Testosterone Therapy Prescription in Men. PLoS ONE 9(1): e85805. doi:10.1371/journal.pone.0085805

ACTIONS

- **Facility Director** (or physician designee): Forward this document to the Facility Chief of Staff (COS).
- **Facility COS and Chief Nurse Executives:** Forward this document to all appropriate providers who prescribe these medications (e.g., **primary care providers, endocrinology, urologists, including contract providers, etc.**). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.
- **ACOS for R&D:** Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).