



### **FDA evaluating risk of stroke, heart attack and death with FDA-approved testosterone products**

#### **Safety Announcement**

**[01-31-2014]** The U.S. Food and Drug Administration (FDA) is investigating the risk of stroke, heart attack, and death in men taking FDA-approved testosterone products. We have been monitoring this risk and decided to reassess this safety issue based on the recent publication of two separate studies that each suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy. We are providing this alert while we continue to evaluate the information from these studies and other available data, and will communicate our final conclusions and recommendations when the evaluation is complete.

At this time, FDA has not concluded that FDA-approved testosterone treatment increases the risk of stroke, heart attack, or death. Patients should not stop taking prescribed testosterone products without first discussing any questions or concerns with their health care professionals. Health care professionals should consider whether the benefits of FDA-approved testosterone treatment is likely to exceed the potential risks of treatment. The prescribing information in the drug labels of FDA-approved testosterone products should be followed.

Testosterone is a hormone essential to the development of male growth and masculine characteristics. Testosterone products are FDA-approved only for use in men who lack or have low testosterone levels in conjunction with an associated medical condition. Examples of these conditions include failure of the testicles to produce testosterone, because of reasons such as genetic problems or chemotherapy. Other examples include problems with brain structures, called the hypothalamus and pituitary that control the production of testosterone by the testicles.

None of the FDA-approved testosterone products are approved for use in men with low testosterone levels who lack an associated medical condition. FDA-approved testosterone formulations include the topical gel, transdermal patch, buccal system (applied to upper gum or inner cheek), and injection.

The first publication that prompted FDA to reassess the cardiovascular safety of testosterone therapy was an observational study of older men in the U.S. Veteran Affairs health system published in the *Journal of the American Medical Association (JAMA)* in November 2013.<sup>1</sup> The men included in this study had low serum testosterone and were undergoing imaging of the blood vessels of the heart, called coronary angiography, to assess for coronary artery disease. Some of the men received testosterone treatment

while others did not. On average, the men who entered the study were about 60 years old, and many had underlying cardiovascular disease. This study suggested a 30 percent increased risk of stroke, heart attack, and death in the group that had been prescribed testosterone therapy.

A second observational study reported an increased risk of heart attack in older men, as well as in younger men with pre-existing heart disease, who filled a prescription for testosterone therapy.<sup>2</sup> The study reported a two-fold increase in the risk of heart attack among men aged 65 years and older in the first 90 days following the first prescription. Among younger men less than 65 years old with a pre-existing history of heart disease, the study reported a two- to three-fold increased risk of heart attack in the first 90 days following a first prescription. Younger men without a history of heart disease who filled a prescription for testosterone, however, did not have an increased risk of heart attack.

We urge health care professionals and patients to report side effects involving prescription testosterone products to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

#### References

1. 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.
2. DOI: 10.1371/journal.pone.0085805