ENDOCRINE SOCIETY
Hormone Science to Health

Endocrine Society Testimony to the
Joint Meeting of the Bone, Reproductive and Urologic Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee
September 17, 2014

Ms. Chairperson and members of the Advisory Committee, thank you for the opportunity to testify today. My name is Dr. Ronald Swerdloff. I appear before you today representing the Endocrine Society. My conflicts include serving as an investigator for NIH and pharmaceutical company sponsored clinical trials for testosterone and testosterone surrogate drugs. I am a member of the Endocrine Society Guidelines Committee for Testosterone Therapy in Men with Androgen Deficiency Syndromes as well as a guideline author for other National and International Societies. The testimony I am about to deliver is the opinion of the Endocrine Society and was developed by a panel of experts in testosterone therapy. The Endocrine Society is the world's largest professional organization of endocrinologists, representing the interests of over 17,500 physicians and scientists engaged in the treatment and research of endocrine disorders.

The Endocrine Society has developed clinical guidelines that provide evidence-based criteria for the diagnosis of testosterone deficiency syndrome in males (male hypogonadism) as well as the recommendations for testosterone replacement therapy and monitoring of treatment.

The diagnosis of male hypogonadism requires both symptoms and signs consistent with testosterone deficiency and consistently subnormal serum level of testosterone on more than one early morning specimen. Many of these symptoms and signs are not specific to testosterone deficiency. Hypogonadism occurs in men of all ages and can be caused by damage to either the testes or the hypothalamic-pituitary axis. Some patients are diagnosed after a specific injury or disease; however, in many instances there is no clear precipitating event or clear-cut anatomical defect. Many drugs and medical conditions are associated with the testosterone deficiency syndrome, which may be reversible with treatment of the co-morbid disease, change in medications or alteration in life style.

We have evaluated the quality of the evidence for diagnosis and treatment of testosterone deficiency syndrome. We recognize that there is a need for more data to better define the appropriate symptoms and signs that characterize the hypogonadal syndrome and define thresholds of serum testosterone required to substantiate a diagnosis of male hypogonadism and justify treatment. We also

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recognize that there is need to standardize and harmonize testosterone assays to reduce the extreme variations in levels measured in different assays.

We are aware of the National Institute of Aging-sponsored Testosterone Trials study evaluating the short-term efficacy of testosterone treatment in older men with hypogonadism. The data, when available from this study, may modify our thinking on the topic; however, these trials were not designed to determine the long-term efficacy and risks of treatment.

We have reviewed the data on cardiovascular risk from testosterone therapy and have concluded that there are inadequate data from well-controlled, adequately powered, interventional studies to determine if testosterone therapy will result in increased, decreased or neutral effects on the cardiovascular system. Similar needs exist regarding risks of testosterone therapy on the prostate gland.

In conclusion:
1) We recommend that treatment with testosterone be limited to men who meet established diagnostic guidelines for hypogonadism,, i.e., men who have clinical manifestations AND consistently low testosterone levels, and that treated patients be monitored as recommended by appropriate guidelines.
2) We also recommend that more data be collected on men of different ages to better establish the serum testosterone thresholds for specific organ-related symptoms and signs, and to determine which clinical manifestations will benefit from replacement testosterone therapy.
3) Finally, we recommend that a large scale, well controlled study be conducted to assess long term cardiovascular and prostate risks associated with testosterone replacement treatment.

Thank you for allowing me to testify on behalf of the Endocrine Society.