

## **GUIDELINE FOR THE OFF-LABEL USE OF TESTOSTERONE (TESTIM® OR TESTOGEL®) IN POSTMENOPAUSAL WOMEN**

**Extracted from the British Menopause Society, Tool for clinicians - Testosterone replacement in the menopause**

[Testosterone replacement in menopause - British Menopause Society \(thebms.org.uk\)](https://www.thebms.org.uk)

### **Introduction**

Testosterone is a normal and important female hormone. Young women produce three to four times the amount of testosterone than they do estrogen. Half of endogenous testosterone and precursors are derived from the ovaries (e.g. androstenedione) and half from the adrenal glands (e.g. dehydroepiandrosterone.)

Some of the effects of testosterone on the body are direct and some due to peripheral conversion to estrogen by aromatase.

Testosterone levels naturally decline throughout a woman's lifespan. Loss of testosterone can be particularly profound after iatrogenic i.e. surgical and medical menopause and premature ovarian insufficiency, but can be significant after natural menopause in some women.

### **What is its role in women?**

Testosterone contributes to libido, sexual arousal and orgasm by increasing dopamine levels in the central nervous system. Testosterone also maintains normal metabolic function, muscle and bone strength, urogenital health, mood and cognitive function. Lack of testosterone in women has been termed Female Androgen Deficiency Syndrome (FADS).

### **What is the impact of testosterone deficiency?**

Distressing sexual symptoms such as low sexual desire, arousal and orgasm can occur when there is testosterone deficiency. It is important to assess other contributory factors such as the psychosexual, physical, iatrogenic and environmental when discussing women's sexual symptoms. Testosterone deficiency can also contribute to a reduction in general quality of life, tiredness, depression, headaches, cognitive problems, osteoporosis and sarcopenia

### **What other effects can testosterone have in the post-menopause?**

After the menopause, estrogen levels fall to undetectable levels. Consequently, the small amount of remaining testosterone may predispose to androgenic symptoms, especially acne, increased facial hair growth and male pattern baldness.

### **Diagnosis and monitoring**

The diagnosis of FADS in the clinical setting should be a pragmatic one based on symptoms

The assessment and interpretation of testosterone levels is problematic, and not available in some primary care settings. Total testosterone is measured, always with sex hormone binding globulin (SHBG) and calculation used to work out the Free Androgen Index (FAI = Total Testosterone x 100 / SHBG).

Although it is not mandatory to perform FAI prior to or for monitoring treatment, it can be useful. A low FAI < 1.0% in women with symptoms of low sexual desire and arousal, supports the use of testosterone supplementation. Repeat estimation at the 3 month follow up visit can be performed to demonstrate if there has been an increase in levels, though clinical response is of paramount importance. It is also useful to demonstrate that values are being maintained within the female physiological range, typically < 5%, thus making androgenic side effects less likely.

There are no testosterone products for female use currently licensed in the UK.

Written by Women's Health Task and Finish Group Feb 2022

Approved by DMAG March 2022

For review March 2024, or before in the light of new/updated guidance or changes to licence

**First choice product: Testim** (1% testosterone, 50 mg testosterone in 5g tube).

Starting dose 1/10th of a tube/day = 5mg/day i.e. each tube should last 10 days.

**Second choice product: Testogel®** (40.5mg testosterone in 2.5g sachet)

Starting dose 1/8th of a sachet/day = 5mg/day i.e. each sachet should last 8 days.

(Please note the Testogel® 50mg testosterone in 5g sachet is being discontinued)

**Application instructions** - Systemic topical use only - A small pea-size amount is applied daily IN THE MORNING, and spread over lower abdomen/upper thighs. The tube can be re-capped or the open sachet should be closed with a clip. It is not necessary to rub it into the skin. The alcohol evaporates and the testosterone is absorbed into the upper layers of the skin. The testosterone is then gradually released into the circulation over the next 24 hours. Allow 3 - 5 minutes to dry before dressing. Wash hands with soap and water after application. The application site should be rotated. Skin contact with partners or children should be avoided until dry.

The loss of sexual desire is complex and may have hormonal, medical, psychosexual and psychosocial aetiologies. Response may not be immediate, taking 8-12 weeks in some instances for the effect to become clinically significant. It is therefore advised that treatment should be trialled for a minimum of 3 months and maximally for 6 months before being discontinued due to lack of efficacy, consider referral to psychosexual or relationship counsellor. Duration of use should be individualised and evaluated at least on an annual basis, weighing up pros and cons according to benefits and risks, as per HRT advice from all menopause societies.

Response to testosterone with regards to efficacy and adverse effects, is highly variable. This is most likely due to varying absorption, metabolism, SHBG levels and sensitivity to testosterone. Not uncommonly, adverse effects occur because healthcare professionals and their patients are confused about the appropriate preparation and dose which should be used in women, due to the lack of specific female preparations and information sheets. Clinical trials have demonstrated that as long as appropriate female physiological doses are prescribed adverse androgenic effects are not problematic and virilising problems do not occur.

Reported adverse effects are shown below; if thought to be linked, the dosage should be reduced or treatment stopped.

- Increased body hair at site of application (occasional problem) – spread more thinly, vary site of application, reduce dosage.
- Generalised Hirsutism (uncommon)
- Alopecia, male pattern hair loss (uncommon)
- Acne and greasy skin (uncommon)
- Deepening of voice (rare)
- Enlarged clitoris (rare)

Randomised controlled trials and meta analyses have not shown an increased risk of cardiovascular disease or breast cancer although longer term trials would be desirable.

When should testosterone be avoided or used with caution?

- During pregnancy or breastfeeding
- Active liver disease
- History of hormone sensitive breast cancer – off label exceptions to this may be agreed in fully informed women with intractable symptoms not responding to alternatives
- Competitive athletes – care must be taken to maintain levels well within the female physiological range
- Women with upper normal or high baseline testosterone levels / FAI.