Testosterone gel for Hypoactive Sexual Desire Disorder (HSDD) in menopausal women.
Guidance for prescribing in Primary and Secondary Care.

GUIDELINE

AMBER Initiated

Testosterone supplementation for low sexual desire in menopausal women may be initiated by specialists in primary or secondary care, including primary care prescribers with a special interest in this area.

Background

Testosterone levels naturally decline throughout a woman's lifespan. Loss of testosterone is particularly profound after iatrogenic i.e. surgical and medical menopause and premature ovarian insufficiency when testosterone production decreases by more than 50%. [1]

Indication and referral by GP

Testosterone supplementation is recommended for restricted use for women in the menopause with Hypoactive Sexual Desire Disorder (HSDD) if Hormone Replacement Therapy (HRT) alone is not effective. Testosterone should only be prescribed for women who complain of low sexual desire after a biopsychosocial approach has excluded other causes such as relationship, psychological and medication related HSDD e.g. SSRIs/SNRIs.

- British Menopause Society guidance on testosterone replacement therapy advises that testosterone contributes to sexual desire by increasing dopamine levels in the central nervous system. [1]
- NICE Guideline (NG23) Menopause Diagnosis and Management 2015 [2] and Clinical Knowledge Summary on Menopause [3] advises primary care clinicians to refer women who have persistent altered sexual function and where hormonal and/or non-hormonal, or non-drug treatments are ineffective to seek specialist advice regarding the use of testosterone supplementation (off-label use).[3]

Prior to referral to a specialist, HRT should be initiated/optimised by the primary care prescriber. If the patient has already been on HRT for 3 to 4 months but demonstrates symptoms of low sexual desire, then referral for testosterone replacement or initiation of therapy by a specialist primary care prescriber can be done at this time.

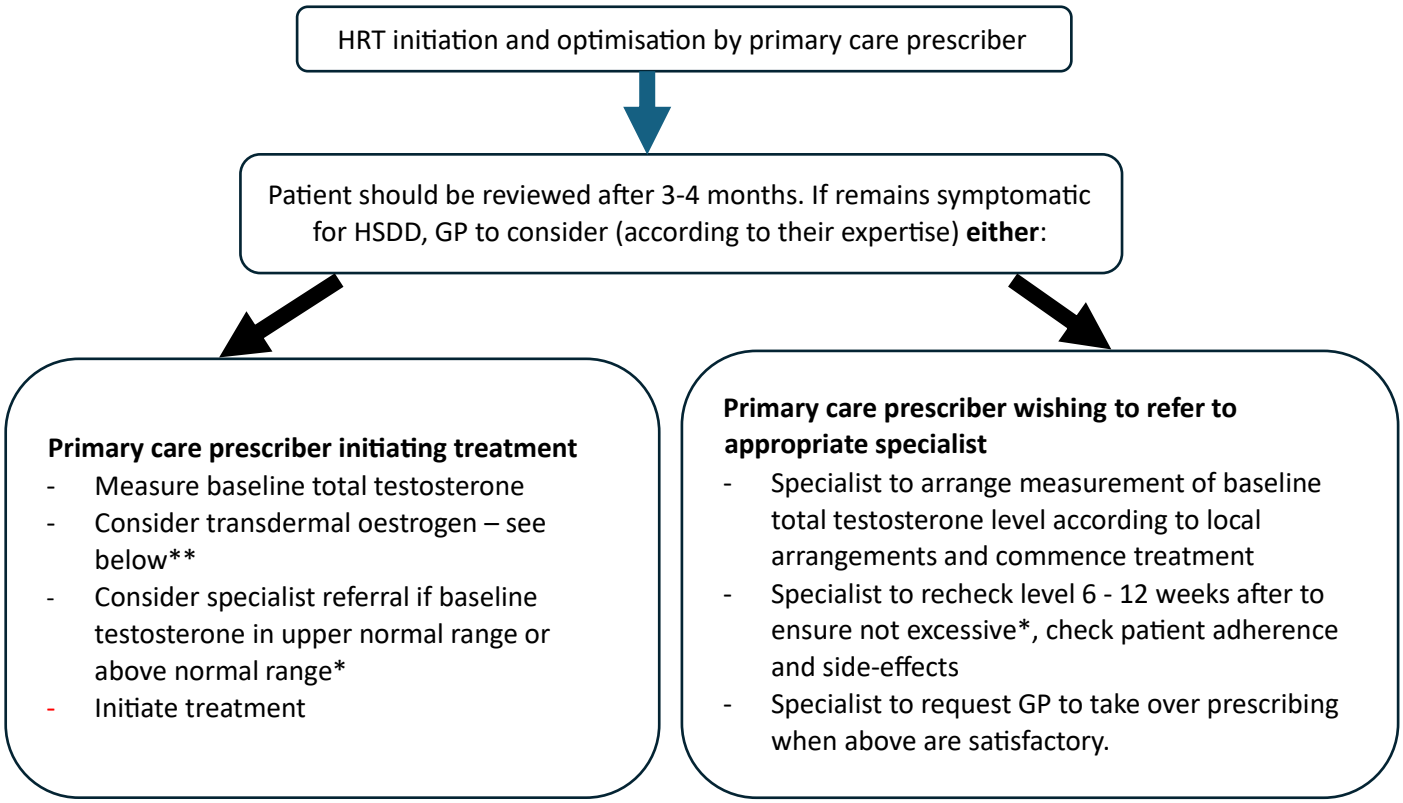
Testosterone levels

Cheshire and Merseyside Pathology Network Reference Range: 0.3-1.2nmol/L (Different laboratories may have different reference ranges).

It is recommended that total testosterone levels are checked by whoever will be initiating testosterone. This will establish a baseline for future monitoring to ensure that levels are not above the reference range before treatment is commenced. Where specialist referral is made the specialist should arrange where possible for total testosterone level to be measured prior to the clinic appointment so that a recent level is available at that point, according to any local arrangements. Testosterone levels should then be rechecked 6 - 12 weeks after commencing therapy by whoever has initiated the treatment. The levels should be reviewed to ensure safety and efficacy of treatment. It is important that monitoring of testosterone levels continues thereafter every 6-12 months to ensure that levels remain within the female reference range in order to minimise adverse effects.[1] This ongoing monitoring can be done by the patient's

GP practice. Testing should be performed as close to the timeline as possible. In cases where levels are within the reference range but patient is symptomatic, the primary care prescriber should consider specialist input as appropriate.

Referral flowchart



* Different laboratories may have different reference ranges.

** Oral oestrogens, especially conjugated oestrogens, can increase serum levels of sex hormone binding globulin. This in turn reduces the effectiveness of testosterone. Switching women with HSDD from oral to transdermal oestrogen can be beneficial as this can increase the proportion of circulating free testosterone without requiring exogenous testosterone[1].

When treating low sexual desire, it is important that urogenital tissues are adequately oestrogenised in women with urogenital atrophy / genitourinary syndrome of the menopause e.g., through use of vaginal oestrogen, to avoid dyspareunia.

Treatments, dosage, and directions for use

Testosterone gel should always be prescribed by brand.

The products and doses which may be prescribed as part of this guideline are:

1st Line:

- Tostran® 2% gel: Dose - 1 metered pump (0.5g of gel is equivalent to 10mg testosterone) on alternate days – each canister should last 240 days· £28.63/60g[4]

2nd Line (only to be used if Tostran pump is unavailable):

- Testogel® 40.5mg/2.5g gel sachets - "small pea sized amount (1/8 of sachet) to be applied daily, 1 sachet should last 8 days. £31.11/30 sachets[4]
- Testavan® 20 mg/g transdermal gel – 1 pump actuation (1.15g of gel is equivalent to 23mg testosterone) twice a week (one 85.5g container should last 37 weeks). £25.22/85.5g[4].

Any variation from the standard (above) dose will result in the patients' care being retained under specialist prescribing. Testosterone is a schedule 4 (part 2) Controlled Drug. Use in women is currently off-label.

Directions for use:
Testosterone gel should be applied to clean, dry, intact skin (lower abdomen/upper thighs). It should be rubbed in gently with one finger until dry, then the application site should be covered, preferably with loose clothing. Skin contact with partners or children should be avoided until the gel is dry and hands should be washed immediately after application. The area of application should not be washed for 2-3 hours after application.

Patient counselling

The specialist initiating treatment is responsible for explaining to the patient that this is an off- label use and it should be clearly documented in the letter from the specialist to the primary care prescriber that the patient has been made aware of this.
The patient should be counselled by the specialist initiating treatment to take precautions to reduce the risk of accidentally transferring testosterone from their skin to another person[5]. The patient should be counselled to wash hands with soap and water after applying the product and to cover the application site with clean clothing once the product has dried. If the product is accidentally transferred to someone else through physical contact, it can lead to increased blood testosterone levels in the other person. It can cause facial and body hair growth, deepening of voice and changes in the menstrual cycle of women, or accelerated height, genital enlargement, and early puberty (including development of pubic hair) in children. The specialist should encourage the patient to be vigilant about implementing measures to minimise risk, to be alert for signs of accidental exposure, and to seek medical advice if accidental exposure is suspected.

Response to testosterone therapy and duration of use

The loss of sexual desire is complex and may have hormonal, medical, psychosexual and psychosocial aetiologies. In clinical trials of women with HSDD, approximately 2/3 of women responded positively to testosterone therapy (compared to 1/3 using placebo). The trials demonstrated that 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. 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.[1]

Transfer of information to the primary care prescriber and length of treatment

Where treatment is not initiated in primary care, the specialist clinician will check a total testosterone level at baseline and initiate testosterone therapy if appropriate. Once dose efficacy and safety has been established, a letter from the specialist will be sent to the GP practice to explain that the patient is stabilised on testosterone in accordance with this guideline. The letter will detail the prescribed dose and frequency, in addition to the date of the next testosterone level check (within 6-12 months). Once the patient is stable, the primary care prescriber can monitor testosterone levels every 6-12 months. The duration of treatment should be individualised and evaluated at least annually as per British Menopause Society advice for HRT[6].

Primary Care Monitoring

The primary care prescriber should monitor total testosterone levels every 6-12 months, in addition to annual assessments of symptom control and adverse effects. Occurrence of adverse effects, particularly those that are rare should raise the possibility with the prescriber that incorrect quantities are being used by the patient. The prescriber should ensure correct administration and review. If adverse effects persist the dosage should be reduced, or treatment stopped, and referral made to the specialist.

Testosterone levels above the normal range should raise the possibility with the prescriber that incorrect quantities are being used by the patient. If high levels persist after administration has been checked, referral to the specialist should be made.

If the patient no longer feels treatment is efficacious in controlling symptoms referral should be made back to the specialist.

Adverse effects of testosterone therapy

Response to testosterone with regards to efficacy and adverse effects is highly variable. This is most likely due to varying absorption, metabolism, and sensitivity to testosterone. Clinical trials have demonstrated that as long as appropriate female physiological doses are used, the adverse androgenic effects are not problematic and virilising problems do not occur.[1]

Occurrence of adverse effects, particularly those that are rare should raise the possibility with the prescriber that incorrect quantities are being used by the patient; the prescriber should ensure correct administration and review. If adverse effects persist the dosage should be reduced, or treatment stopped, and referral made to specialist.

Patient education is important to ensure correct technique and recognition of adverse effects which should be reported to their primary care prescriber.

Adverse effects: [1]

- Increased body hair at site of application (occasional problem) – spread more thinly, vary site of application, reduce dosage.
- Generalised hirsutism (uncommon)
- Acne and greasy skin (uncommon)
- Enlarged clitoris (rare)

Irreversible:

- Alopecia, male pattern hair loss (uncommon)
- Deepening of voice (rare)

More data are required for the long-term effects on cardiovascular and breast outcomes but the short-term data from a recent meta-analysis are reassuring.

Contraindications: [1]

- Pregnancy or breastfeeding
- Active liver disease
- Hypercalcaemia
- Women with known upper normal or high baseline testosterone levels / Free Androgen Index (FAI).

Cautions: [1]

- History of hormone sensitive breast cancer – 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. Seek specialist advice.

For further information about testosterone consult the BNF and the product SPC. [4,7]

References

1. British Menopause Society, Testosterone replacement in menopause 2022. [Accessed on 20/02/2024]
2. National Institute of Clinical Effectiveness (NICE). Menopause diagnosis and management 2015 (NG23). Available via [Accessed on 20/02/2024]
3. NICE Clinical Knowledge Summaries (CKS); Menopause. 2020. [Accessed on 20/02/2024]
4. Electronic Medicines Compendium (EMC). Summary of Product Characteristics, Tostran [Kyowa Kirin Ltd], Testogel [Besins Healthcare (UK) Ltd], Testavan [The Simple Pharma Company Limited]. [Accessed on 20/02/2024]
5. MHRA. Drug Safety Update: Topical Testosterone (Testogel): risk of harm to children following accidental exposure. Volume 16, issue 6: 2023: 2. [Accessed on 20/02/2024]
6. British Menopause Society, HRT – Guide 2020 [Accessed on 20/02/2024]
7. Joint Formulary Committee. British National Formulary London: BMJ and Pharmaceutical Press. [Accessed on 20/02/2024]

Further reading

- Achilli C, Pundir J, Ramanathan P, Sabatini L, Hamoda H, Panay N. Efficacy and safety of transdermal testosterone in postmenopausal women with hypoactive sexual desire disorder: a systematic review and meta-analysis. Fertil Steril. 2017; 107(2):475-482.
- Maclaran K, Panay N. The safety of postmenopausal testosterone therapy. Women's Health (Lond Engl). 2012 8(3):263-75.
- Guys & St Thomas NHS Foundation Trust. Hormone Replacement therapy. Patient Leaflet.