Topical testosterone for management of Low libido in menopausal and post menopausal women (unlicensed indication)

Traffic light classification- Green - Can be initiated and prescribed in all care settings (including primary care)

Information sheet for Primary Care Prescribers

Indication: Management of Low Libido in Menopausal (both natural and surgical) and post menopausal women (unlicensed indication)

Therapeutic Summary:

The role of androgens in maintaining well-being in women is not fully understood. Testosterone is an important female hormone. Healthy young women produce approximately 100 – 400 mcg per day. Between a women's mid 30's and early 60's, adrenal androgen production reduces by about two-thirds. After a natural menopause, ovarian production continues to a varying degree. After bilateral oophorectomy, ovarian production of androgens and precursor sex hormones is lost. It has been suggested that there is a link between low circulating concentrations of testosterone and reduced sexual functioning in postmenopausal women.

In postmenopausal women who are distressed by low libido and who have no other identifiable cause (e.g. physical and psychosocial factors and medications), testosterone therapy if HRT alone is not effective can be considered. National institute for Health and Care Excellence (NICE) Guideline NG23 Menopause: diagnosis and management states - Consider testosterone supplementation for menopausal women with low sexual desire if HRT alone is not effective. The British Menopause Society (BMS), A new tool for clinicians: Testosterone replacement in menopause states: The loss of sexual desire is complex and may have hormonal, medical, psychosexual and psychosocial aetiologies. In clinical trials of women with low libido, 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.

Before initiating the treatment

- Investigate other causes of low libido, these include physical and psychosocial factors and medications, and HRT alone is not effective.
- It is recommended that total testosterone levels are checked before treatment to establish a baseline for future monitoring and to ensure that levels are not in the upper range before treatment is commenced.
- Free testosterone assays are not recommended in this context as correlation with biological activity of testosterone has not been confirmed. Clinical assessment of potential adverse effects is equally important as some women are more sensitive to physiological levels of androgens
- It is also recommended by some guidelines that testosterone levels are reassessed at 3-6 weeks after treatment is commenced, but given that most national health service clinics

review their patients after 2-3 months it is recognised that this is an aspirational goal and that testing should be performed as close to this timeline as possible.

- It is important that monitoring continues every 6-12 months to ensure that levels remain within the female physiological range in order to minimise adverse effects.
- Samples should be collected early morning (8am to 11am)
- Results should be interpreted with caution in the presence of abnormal albumin levels
- Ensure that women are on HRT before and while taking testosterone.

Testosterone Treatment

- Tostran® [Kyowa Kirin Ltd] (2% testosterone gel in a canister containing 60g)
  Dose 1 metered pump of 0.5g of gel = 10 mg of testosterone10mg on alternate days – each canister should last 240 days.).
  Patients should require between 1-2 canisters per year dependent on dose, any requests above this should trigger a review with the patient.

  OR

- Testim® tubes (1% testosterone gel) – 5g tube containing 50mg testosterone. Apply 1/10th (e.g. a small pea amount) of a tube once daily (5mg daily dose), replace screw lid between uses.One tube should last for 10 days.

This is an unlicensed indication.

Administration

The British Menopause Society recommends: “The testosterone gel/cream should be to be applied to clean dry skin (lower abdomen/upper thighs) and allowed to dry before dressing. Hands should be washed with soap and water after applications. Skin contact with partners or children should be avoided until dry and hands should be washed immediately after application. The area of application should not be washed for 2-3 hours after application.”

Duration of treatment

- Testosterone therapy should be considered as a clinical trial, which should not be continued if a woman has not experienced a significant benefit by 3 months.
- Usually treatment takes up to 3 months to be effective, so a 3 month follow up is arranged and then 3 monthly follow up appointments continue until a woman is established on treatment.
- 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.

Contraindications

- During pregnancy and breastfeeding
- Hypersensitivity to the active substance(s) or to any of the excipients listed in the product

Cautions

- Severe cardiac, hepatic, or renal insufficiency or ischaemic heart disease; as may cause severe complications characterised by oedema with or without congestive cardiac failure, hypertension as testosterone may cause a rise in blood pressure
- Caution in renal and hepatic impairment.
- Testosterone may potentiate sleep apnoea in some patients, especially those with risk factors such as obesity or chronic lung disease.
- Caution with skeletal metastases due to the risk of hypercalcaemia/hypercalciuria developing from androgen therapy.
- Epilepsy and migraine
- Thrombophilia; some post-marketing studies and reports of thrombotic events
- Competitive athletes – care must be taken to maintain levels well within the female physiological range
- Women with upper level or high baseline testosterone levels / FAI.
- Risk of testosterone transfer: close skin contact with the area of application by a partner or child should be avoided.
- Randomised studies have not shown an increased risk of cardiovascular disease or breast cancer with testosterone replacement although longer term follow up studies are lacking.

Drug Interactions

- **Anticoagulants**: the anticoagulant effect can increase. Patients receiving warfarin require close monitoring of their INR especially when the androgen treatment is started, stopped or the dose is changed**.**
- Concurrent administration of testosterone with tetracosactide, (**ACTH) or corticosteroids** may increase the likelihood of oedema; thus these drugs should be administered with caution, particularly in patients with cardiac, renal or hepatic disease.
- Androgens may decrease concentrations of thyroxin-binding globulin, resulting in decreased total T4 serum concentrations and increased resin uptake of T3 and T4. Free thyroid hormone concentrations remain unchanged however, and there is no clinical evidence of thyroid dysfunction.

Monitoring requirements

- Monitoring of testosterone therapy specifically should include subjective assessments of sexual response, desire, and satisfaction as well as evaluation for potential adverse effects.
- Recommended by some guidelines that testosterone levels are reassessed at 3-6 weeks after treatment is commenced, but given that most national health service clinics review their patients after 2-3 months it is recognised that this is an aspirational goal and that testing should be performed as close to this timeline as possible.

- It is important that monitoring continues every 6-12 months to ensure that levels remain within the female physiological range in order to minimise adverse effects.
- Monitor for symptoms of excessive androgen exposure such as irritability, nervousness, weight gain.
- British Association for Sexual Health and HIV BASHH) Guidelines state that it is good practice to measure fasting lipid and glucose levels after six months of therapy, if clinically indicated (e.g. by diabetes or hyperlipidaemia).

Adverse effects

- 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)

References

1) National Institute of Health and Care Excellence (NICE) Guidelines [NG23]: Menopause: diagnosis and management. Last updated December 2019.
2) NICE Clinical Knowledge Summary: Menopause Last revised November 2020.
3) General Medical Council (GMC): Good practice in prescribing and managing medicines and devices (2013).
4) Medicines and Healthcare products Regulatory Agency (MHRA): Off-label or unlicensed use of medicines: prescribers' responsibilities. https://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities
5) British Society for Sexual Medicine. Guidelines on the management of sexual problems in women: the role of androgens [Internet]. 2010 [cited 2016 Jan 20]. Available from: https://www.bashhguidelines.org/media/1096/3117.pdf
6) British Menopause Society: Testosterone replacement in menopause May 2022– tools for clinicians.
7) Coventry & Warwickshire Area Prescribing Committee Drug Position Statement: Transdermal Testosterone for low libido in Menopausal (both natural and surgical) Females (Oct 19) https://www.covwarkformulary.nhs.uk/docs/chapter06/DPS098-Testosterone%20transdermal%20preparation.pdf?UNLID=92004236520217210959
8) Clayton et al; Mayo Clin Proc 2018 Apr;93(4):467-487
International Society for the Study of Women's Sexual Health Process of Care for Management of Hypoactive Sexual Desire Disorder in Women
https://www.mayoclinicproceedings.org/article/S0025-6196(17)30799-1/fulltext

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