AMBER 1 GUIDANCE FOR TOPICAL TESTOSTERONE FOR MANAGEMENT OF LOW LIBIDO IN MENOPAUSAL AND POST-MENOPAUSAL WOMEN

Traffic light classification – AMB1

PLEASE NOTE: THIS GUIDELINE DOES NOT INCLUDE THE USE OF TOPICAL TESTOSTERONE FOR THE MANAGEMENT OF OTHER MENOPAUSAL SYMPTOMS IN WOMEN (RED DRUG)

Information sheet for Primary Care Prescribers

1.Background

Indication: Management of Low Libido in Menopausal (both natural and surgical) and postmenopausal women

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 microgram 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.

There are various preparations, all licensed for use in men in the UK, that can be used to treat women outside of product license. It is important that this information is recorded in the patients' records.

Before initiating treatment

- **Investigate other causes of low libido, these include physical and psychosocial factors and medications.** Optimise HRT and exclude relationship issues.
- It is important that any symptoms of vulvovaginal atrophy are also adequately treated if testosterone is being considered for Hypoactive Sexual Desire Disorder (HSDD).
- Ensure that women are on HRT before and while taking testosterone:
    - The NICE Menopause Guideline (NG23) and the BMS recommend that a trial of conventional HRT is given before testosterone supplementation is considered.
    - Oral oestrogens, especially conjugated oestrogens, can reduce the effectiveness of testosterone by increasing sex hormone binding globulin levels. 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.
- **Monitoring** - It is recommended that total testosterone levels are checked before treatment to establish a baseline for future monitoring and to ensure that levels are within the reference range provided by the lab before treatment is commenced.

4. Dose/Duration

Most testosterone products are off label/license for female usage and may not always be available

- Testogel [Besins Healthcare UK] (2.5g sachets containing 40.5mg testosterone): Starting dose 1/8 of a sachet/day = approx. 5mg/day – product of choice
- Tostran [Kyowa Kirin Ltd] (2% testosterone gel in a canister containing 60g) : Starting dose 1 metered pump of 0.5g = 10mg on alternate days – 2nd line choice

Testogel sachets–

- Average of 0.5ml – 1ml per day (a large pea sized blob applied to the lower abdomen/tops of top of thighs) i.e. 1 x sachet per 8 days
  Thirty sachets per box. Patients should require 2 boxes of 30 sachets per year

- Administered by the patient herself, onto clean, dry, healthy skin on the sites (abdomen/top of thighs). Applied immediately onto the skin. Allow drying for at least 3-5 minutes before dressing. Wash hands with soap and water after applications.

Tostran Gel Pump

- Starting dose 1 metered pump of 0.5g of gel = 10 mg of testosterone twice a week (each canister should last 120 doses). This can be increased to three times a week if required.
  Patients should require between 1-2 canisters per year dependent on dose, any requests above this should trigger a review with the patient.
- Administered by the patient herself, onto clean, dry, healthy skin on the sites indicated by the manufacturer. Applied immediately onto the skin. Allow drying for at least 3-5 minutes before dressing. Wash hands with soap and water after applications.

5. Duration of treatment

- Testosterone therapy should be considered as a 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 three 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.

6. Contraindications and Cautions

Contraindications

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

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 (see local reference ranges provided by lab).

- 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.

6. Drug interactions

The following drugs are known or suspected interactions:	
Interacting Drug	Advice
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.
ACTH or corticosteroids	Concurrent administration of testosterone with **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.
Levothyroxine	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
Diabetic medication	Improved insulin sensitivity, glucose tolerance, glycaemic control, blood glucose and glycosylated haemoglobin levels have been reported with androgens. In diabetic patients, the dose of antidiabetic medications may need reduction.
Misc.	The application of sunscreen or lotion does not reduce efficacy

The common effects and interactions lists above are not exhaustive. For further information always check with BNF at www.medicinescomplete.com

or SPC (www.medicines.org.uk). (Registration may be required for both.)

7. 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.
- Monitor for symptoms of excessive androgen exposure such as irritability, nervousness, weight gain.
- Monitor total testosterone levels at baseline, 3 months, 6 months, then annually thereafter to ensure they remain within the normal reference range provided by the lab.
- Blood Pressure monitoring should be checked annually if taking HRT.
- FBC for polycythaemia, U&E, LFT, bone profile for calcium level, renal function and hepatic function, lipid profile 12 monthly

- **STOP TREATMENT and refer to specialist if haematocrit above the upper reference range provided by the lab or abnormal liver function tests develop.**

8. 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)

9. Information given to patients

See BMS patient information leaflet available at https://www.womens-health-concern.org/wp-content/uploads/2022/12/22-WHC-FACTSHEET-Testosterone-for-women-NOV2022-B.pdf

Important safety information

MHRA/CHM advice: Topical testosterone (Testogel®): risk of harm to children following accidental exposure (January 2023)

The CHM has reviewed reports of topical testosterone being repeatedly accidentally transferred to children, resulting in genital enlargement and premature puberty due to increased blood-testosterone levels. Repeated accidental exposure in adult females may also result in facial and/or body hair growth, deepening of voice, and menstrual cycle changes.

Healthcare professionals are advised to counsel patients or their carers on:

- the risks and possible side-effects of accidental transfer of topical testosterone to others;
- methods to reduce these risks, such as washing hands with soap and water after application, covering the application site with clean clothing once the gel has dried, and washing the application site with soap and water (after the recommended time period) before physical contact with others;
- being alert for signs of accidental exposure, and to seek medical advice if this is suspected.

Cost of treatment (October 2024)

Testogel 40.5mg/2.5g transdermal gel sachets (30 sachets - £31.11) Cost per 28 days: £4.15

Tostran® pump (testosterone 2% gel) 10 mg per actuation 60g (£28.63) Cost per 28 days:

£3.34

References

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4. NICE Clinical Knowledge Summary: Menopause Last revised September 2022.
5. General Medical Council (GMC): Good practice in prescribing and managing medicines and devices (2013).
6. Medicines and Healthcare products Regulatory Agency (MHRA): Off-label or unlicensed use of medicines: prescribers' responsibilities. https://www.gov.uk/drugsafety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities
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8. British Menopause Society: Testosterone replacement in menopause - tools for clinicians.
9. Coventry & Warwickshire Area Prescribing Committee Drug Position Statement: Transdermal Testosterone for low libido in Menopausal (both natural and surgical) Females (Oct 19) DPS098-Testosterone transdermal preparation.pdf (covwarkformulary.nhs.uk)
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11. Topical testosterone (Testogel): risk of harm to children following accidental exposure - GOV.UK (www.gov.uk)
12. https://www.womens-health-concern.org/wp-content/uploads/2022/12/22-WHC-FACTSHEET-Testosterone-for-women-NOV2022-B.pdf

AMBER 1 GUIDANCE

Humber Area Prescribing Committee

Document and version control	**This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the SPC (data sheet) or BNF for further prescribing information.**		
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1	Natasha Suffill	Clinical Lead Pharmacist, CHCP Medicines Service	New document – adapted from NY&Y guidance