SHARED CARE GUIDELINE

Drug: Testosterone (transdermal)

As supplementation for **postmenopausal women** with low sexual desire if HRT alone is not effective

(For information relating to the prescribing of **testosterone for other indications please visit** www.lancsmmg.nhs.uk)

Introduction	**Licensed indication:**[1] None covered – see separate shared care guidance. **Off-label indication:** As supplementation for postmenopausal women with low sexual desire if HRT alone is not effective **Please note:** Long term safety data (i.e. more than 2 years exposure) for treatment with testosterone in women with natural menopause is very limited, particularly for women not on hormone therapy. Shared care must only continue beyond 2 years if, following discussion with the patient 2 years post initiation, the specialist confirms that treatment can continue. **Clinical Background:**[2] Testosterone is an important female hormone. Healthy young women produce approximately 100 – 400 mcg per day. This represents three to four times the amount of estrogen produced by the ovaries. Testosterone levels naturally decline throughout a woman's lifespan. 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. Testosterone deficiency can lead to a number of distressing sexual symptoms such as low sexual desire, arousal and orgasm. Testosterone deficiency can also contribute to a reduction in general quality of life, tiredness, depression, headaches, cognitive problems, osteoporosis and sarcopenia. **Background to shared care arrangements:** The best interest, agreement and preferences of the patient should be at the centre of any shared care agreement and their wishes followed wherever possible. Patients should be able to decline shared care if, after due consideration of the options, they decide it is not in their best interests. **Please note:** The provision of shared care prescribing guidelines does not necessarily mean that the GP must agree to and accept clinical and legal responsibility for prescribing; they should only do so if they feel clinically confident in managing that condition. Referral to the GP should only take place once the GP has agreed to this in each individual case, and the hospital or specialist will continue to provide prescriptions until a successful transfer of responsibilities has occurred. The GP should confirm the agreement and acceptance of the shared care prescribing arrangement and that supply arrangements have been finalised. The secondary/tertiary provider must supply an adequate amount of the medication to cover the transition period. The patient should then be informed to obtain further prescriptions from the GP. **This shared care guideline excludes:**

	1. Testosterone replacement for hypogonadism due to testosterone deficiency in adult men 2. Hormone therapy in gender dysphoria (Prescribing for trans men (this applies to a person assigned female, cis-female, at birth undertaking gender transition to become a male)
Form	Gel for transdermal application
Dose and administration (please refer to BNF / SPCs for full details)	**Use of these products is unlicensed for the indication of supplementation for postmenopausal women with low sexual desire if HRT alone is not effective.** Please refer to the Guidelines for Good Prescribing in Primary Care for advice on prescribing for unlicensed indications. Tostran should be considered before other preparations as the dose is measurable. **Current (unlicensed) treatment options that can be used to deliver precise dosing:** **Tostran® 2%** gel in cannister[3] Each full depression of the canister piston delivers one half gram of gel (10 mg testosterone). Recommended dose is one full depression of the canister piston (10 mg testosterone) on alternate days.[2,4] **Testogel 40.5mg** transdermal gel sachets[5] Starting dose 1/8 of a sachet/day (approximately pea sized amount of gel) = approx. 5mg/day i.e. each sachet should last 8 days.[6] **Application instructions:** For this patient cohort, testosterone gel should be applied to clean dry skin (lower abdomen/upper thighs; rotate site of application) an) and allowed to dry before dressing.[7] Skin contact with partners or children should be avoided until dry and hands should be washed diately after application (see 'contraindications/cautions' for more information).[2] **Individual product summary of product characteristics (SPCs) or patient information leaflets (PILs) should be consulted for further product information. Note that the dosage instructions in these documents are not applicable to this indication. Advise female patients that the information contained in the PIL supplied with the product is produced for male patients for a different indication and may not be applicable to them.**
Common Adverse Effects (please refer to BNF / SPCs for full details)	When used for low sexual desire in post-menopausal women the long-term (more than 2 years exposure) effects of testosterone are largely unknown, but side-effects can include growth of unwanted hair (general and/or at site of application), frontal balding and deepening of the voice. **Longer term trials are needed to establish the long term safety profile of testosterone in this patient population, particularly to establish if there is any increased risk of cardiovascular disease or breast cancer.** The following side effects will largely have been observed in the male population: **Common or very common**

	Hot flush; hypertension; polycythaemia; skin reactions including application site reactions (including erythema, rash and pruritus); weight increased, Hypertriglyceridaemia; Acne **Uncommon** Alopecia; asthenia; behaviour abnormal; depression; dizziness; dyspnoea; dysuria; gynaecomastia; headache; hyperhidrosis; insomnia; nausea; sexual dysfunction; peripheral oedema; pruritus **Rare or very rare** Pulmonary oil microembolism; enlarged clitoris **Frequency not known** Anxiety; epiphyses premature fusion; fluid retention; jaundice; liver function test abnormalities; oedema; paraesthesia; precocious puberty; seborrhoea; sleep apnoea; urinary tract obstruction, Anaemia; deep vein thrombosis; electrolyte imbalance (retention of sodium, chloride, potassium, calcium, inorganic phosphate and water); frontal balding (in women); hair growth unwanted (in women); hypertrichosis; malaise; muscle cramps; musculoskeletal pain; vasodilation; voice lowered (in women); nausea; Altered blood lipid levels, reduction in HDL cholesterol and weight gain **Please refer to the SPC or BNF for full list.**
Contraindications / Cautions (please refer to BNF / SPCs for full details)	**Contraindications:**[1,2,3,Error! Bookmark not defined.,7] • Breast cancer • Endometrial cancer • History of liver tumours • Hypercalcaemia • Known hypersensitivity to the active substance or any of the excipients listed in the SPC (see individual product SPCs) • Pregnancy • Breast-feeding • In the absence of long-term safety data, women with cardiovascular disease and/or uncontrolled hypertension should not be prescribed testosterone. **Cautions:**[**Error! Bookmark not defined.**,1,3,7] Elderly; Epilepsy; Migraine; Sleep apnoea; Cardiac impairment: In patients suffering from severe cardiac, hepatic or renal insufficiency or ischaemic heart disease, treatment with testosterone may cause severe complications characterised by oedema with or without congestive cardiac failure. In such case, treatment must be stopped immediately; Hypertension: Testosterone may cause a rise in blood pressure and this medicine should be used with caution in patients with hypertension; Diabetes mellitus: Improved insulin sensitivity may be observed in patients treated with androgens and may require a decrease in the dose of antidiabetic medications. Monitoring of the glucose level and HbA1c is advised for patients treated with androgens; Skeletal metastases: Risk of hypercalcaemia or hypercalciuria (if this occurs, treat appropriately and restart treatment once normal serum calcium concentration restored); Polycythaemia: Stop treatment or reduce dose if severe polycythaemia occurs;

	Tumours: Risk of hypercalcaemia or hypercalciuria (if this occurs, treat appropriately and restart treatment once normal serum calcium concentration restored); Thrombophilia: Increased risk of thrombosis. Testosterone should be used with caution in patients with thrombophilia or risk factors for venous thromboembolism (VTE), as there have been post-marketing studies and reports of thrombotic events (e.g. deep-vein thrombosis, pulmonary embolism, ocular thrombosis) in these patients during testosterone therapy. In thrombophilic patients, VTE cases have been reported even under anticoagulation treatment, therefore continuing testosterone treatment after first thrombotic event should be carefully evaluated. In case of treatment continuation, further measures should be taken to minimise the individual VTE risk. **The attention of athletes is drawn to the fact that testosterone may produce a positive reaction in anti-doping tests.** Potential testosterone transfer: If no precaution is taken, testosterone gel can be transferred to other persons by close skin to skin contact, resulting in increased testosterone serum levels and possibly adverse effects (e.g. growth of facial and/or body hair, deepening of the voice, irregularities of the menstrual cycle) in case of repeat contact (inadvertent androgenisation). The patient should be informed about the risk of testosterone transfer and about safety instructions present in the PIL. Testosterone gel should not be prescribed in patients with a major risk of non-compliance with safety instructions (e.g. severe alcoholism, drug abuse, severe psychiatric disorders). This transfer is avoided by wearing clothes covering the application area or showering prior to contact. See product literature for advice on washing after application of testosterone, as advice differs between products. Pregnant women must avoid any contact with this medicine application sites. In case of pregnancy of the partner, the patient must reinforce their attention to the precautions for use.
Potentially Serious Drug Interactions (please refer to BNF / SPCs for full details)	All oral estrogens (oral contraceptives and oral HRT) will result in an increase in SHBG which will bind testosterone and reduce bioavailability. The concurrent use of tibolone or glucocorticoids with testosterone may result in elevated testosterone levels due to a decrease in SHBG. Concurrent administration with ciclosporin may result in increased ciclosporin toxicity and elevated cyclosporin blood levels. **Oral anticoagulants** Changes in anticoagulant activity (the increased effect of the oral anticoagulant by modification of coagulation factor hepatic synthesis and competitive inhibition of plasma protein binding): Increased monitoring of the prothrombin time, and INR determinations, are recommended. Patients receiving oral anticoagulants require close monitoring especially when androgens are started or stopped. **Corticotrophin (ACTH) and corticosteroids** Concomitant administration of testosterone and ACTH or corticosteroids may increase the risk of developing oedema. As a result, these medicinal products should be administered cautiously, particularly in patients suffering from cardiac, renal or hepatic disease. **Interaction with laboratory tests**

	Androgens may decrease levels of thyroxin binding globulin, resulting in decreased T4 serum concentrations and in increased resin uptake of T3 and T4. Free thyroid hormone levels, however, remain unchanged and there is no clinical evidence of thyroid insufficiency. **Diabetic Medication** See notes under 'Contraindications/Cautions'
Secondary Care AND BMS accredited NHS GPs, pharmacists and nurses responsibilities	1) Testosterone therapy must be initiated by a menopause specialist in secondary care following confirmation of the diagnosis of Hypoactive sexual desire disorder/dysfunction (HDSS) after full clinical assessment. Other factors contributing to HDSS must be identified and addressed before testosterone therapy is initiated. **Please note:** LSCMMG have agreed that BMS (British Menopause Society) accredited **NHS GPs, pharmacists and nurses** can also commence testosterone for postmenopausal women with low sexual desire if HRT alone is not effective in primary care – **see below for full details.** 2) Testosterone therapy must only be considered if HRT alone has proven ineffective. 3) Record the person's preferences and concerns in their treatment plan. Patients should be able to decline shared care if, after due consideration of the options, they decide it is not in their best interests. Patients should provide explicit consent and this should be recorded in both the patients notes and on the shared care agreement form. 4) Provide information about the medication to patients, including common side effects, necessary monitoring, and where that monitoring will take place. Also, to keep the patient informed of the process at all stages to ensure continuity of treatment. 5) Women must be counselled on the absence of long term safety data for the use of testosterone in women. 6) Women must be counselled on the unlicensed nature of the testosterone products available and the implications of this. 7) Titrate the dose against symptoms and adverse effects until dose optimisation is achieved, that is, reduced symptoms etc. 8) Continue all necessary physical health monitoring and monitor effectiveness of medication for and adverse effects, and document in the person's notes. 9) Prescribe and monitor the patient for a minimum period of three months and until the patient is on a stable dose. 10) Continue to provide prescriptions until a successful transfer of responsibilities to the GP has occurred. The secondary/tertiary provider must supply an adequate amount of the medication to cover the transition period. 11) Once Part 2 of the Shared Care Agreement Form has been returned completed and signed by the patients GP, the patient should then be informed to obtain further prescriptions from the GP after the transition period and must be made fully aware of all necessary monitoring requirements. 12) Conduct an annual face to face medication review for all patients covered by this shared care guidance. A decision should communicated to the GP 2 years post initiation, following discussion with the patient about the relative risk and benefits of therapy, if treatment is to continue beyond 2 years. 13) Contact the GP within 3 days of a patient missing a specialist face to face appointment to advise whether treatment should be withheld 14) Accept referrals back from primary care for medication discontinuation. 15) Resume prescribing and monitoring of the patient when a decision for managed withdrawal of treatment has been taken.

	16) Continue to provide emergency appointments where patients are receiving prescriptions from their GP and they feel that a prompt assessment or review of their treatment is required. 17) Provide prompt on-going advice to General Practitioners as required without necessarily requiring a new referral. 18) Provide advice to the GP as to the changes in parameters that should trigger urgent referral back to the specialist 19) Telephone details and (if appropriate) secure email addresses for both Secondary and Primary Care should be exchanged and recorded. This should include out-of-hours contact numbers. Patients and their carers should also be provided with contact details for support and help if required; both in and out of hours. 20) Ensure that adequate training and educational support is in place for the primary care multidisciplinary team (in collaboration with the local commissioner of the service pathway i.e. CCG). **Please note:** LSCMMG have agreed that BMS (British Menopause Society) accredited **NHS GPs, pharmacists and nurses** can commence testosterone for postmenopausal women with low sexual desire if HRT alone is not effective in primary care. BMS accredited **NHS GPs, pharmacists and nurses** can then enter into a shared care agreement with the patient's own GP (if required) for continuing care. The responsibilities defined above in this section apply to both secondary care prescribers AND BMS accredited **NHS GPs, pharmacists and nurses**. For clarity, a BMS menopause specialist is a healthcare professional who holds a recognised menopause educational qualification: • BMS Advanced Certificate in the Principles and Practice of Menopause Care • RCOG/BMS Advanced Training Skills Module (ATSM) in menopause care • FSRH Menopause Care Professional Diploma (MCPD) • FSRH Advanced Certificate in Menopause Care • FSRH Community Sexual & Reproductive Healthcare (CSRH) curriculum, obtaining the Certificate of Completion of Training (CCT), or reaching the equivalent standard as assessed by the GMC and awarded a CESR in CSRH; or an equivalent qualification (e.g. menopause and POI module of the subspecialty training programme in reproductive medicine) **AND** who: • is a member of the British Menopause Society, **and** • attends a national or international menopause society scientific conference at least once every three years (e.g. BMS, IMS, EMAS), **and** • provides a minimum of 100 menopause-related consultations per year, of which at least 50 are new; **and** • is responsible for ensuring that the specialism is documented in their job plan and is discussed and recorded at their annual appraisal in the UK or Ireland.
Primary Care Responsibilities	**Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.** 1) To consider requests to prescribe under shared care arrangements and reply in a timely manner by completing, signing and returning Part 2 of the Shared Care Agreement Form. 2) To provide continuation prescriptions or identify any concerns about the request to the prescriber in the specialist team. It is expected that primary care

	prescribers will not make changes to the dose/formulation, unless it is in consultation with the specialist team. 3) As testosterone is a schedule 4 controlled drug, the prescribed quantity should not exceed 30 days; exceptionally, to cover a justifiable clinical need and after consideration of any risk, a prescription can be issued for a longer period, but the reasons for the decision should be recorded on the patient's notes. 4) To monitor the patient as outlined below and contact the specialist team if results give rise to concern. Any ongoing monitoring requirements for individual patients discharged from secondary care will be identified by the specialist service as part of the discharge information to the GP. 5) To contact specialists within the team where concerns arise about a patient's presentation or when advice is needed. 6) To refer to secondary care if withdrawal of treatment might be indicated. **Circumstances for discontinuation of treatment in Primary Care** 1) As a joint decision with specialist team providing specific advice in case of adverse effect pending assessment. 2) Following non-attendance at annual specialist team review pending that review taking place or if there is failure to engage with the review process. 3) Patient wishes to discontinue testosterone treatment.

Monitoring

Secondary care should prescribe and monitor the patient for a minimum period of three months and until the patient is on a stable dose.

Monitoring Required	Schedule
Haematocrit	Monitored at baseline, 3 months, 6 months, then annually thereafter if no concerns.
Haemoglobin	Monitored at baseline, 3 months, 6 months, then annually thereafter if no concerns.
LFTs	Monitored at baseline, 3 months, 6 months, then annually thereafter if no concerns.
Lipids	Monitored at baseline, 3 months, 6 months, then annually thereafter if no concerns.
HbA1c and blood glucose in patients with DM	Manage according to local guidelines and patients diabetes management plan.
Breast care	Attend breast screening appointments as per national policy.
Testosterone	Clinical response (efficacy) Clinical response may take 8-12 weeks. Assess clinical response at 3 months and 6 months. If no benefit is experienced by 6 months, treatment should be ceased. If treatment continues then assess clinical response at least annually. Patients should be monitored for signs of androgen excess. Androgen levels (safety) Testosterone levels should not be used to diagnose HSDD. Free Androgen Index (FAI) should be calculated using the following equation at baseline, 3 months, then every 6 months if treatment continues: **Free Androgen Index = Total Testosterone x 100 / SHBG** Request testosterone and sex hormone binding globulin (levels should be taken in the morning before the gel is applied). Check FAI 3 months after any dose change. FAI should be maintained within the female physiological range (typically < 5%).[2]
Blood pressure	Manage according to local guidelines.

Version Number	Date	Amendments Made	Author
1.0	August 2022	New document.	JG/AGR
1.1	June 2024	BMS accreditation added.	AGR
1.2	September 2024	Testosterone sachets added	PT
1.3	April 2025	Application instructions clarified and BMS accredited initiation made clearer.	AGR

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References

[1] Electronic Medicines Compendium, "Summary of Product Characteristics Testogel 50mg, transdermal gel in sachet," Besins Healthcare (UK) Ltd, March 2021 [Online]. Available: https://www.medicines.org.uk/emc/product/6808/smpc [Accessed Jan 2022].

[2] British Menopause Society, “Testosterone Replacement in Menopause”, Feb 2019 [Online]. Available: https://thebms.org.uk/publications/tools-for-clinicians/testosterone-replacement-in-menopause/#:~:text=Testosterone%20is%20an%20important%20female,estrogen%20produced%20by%20the%20ovaries.&text=Testosterone%20levels%20naturally%20decline%20throughout%20a%20woman's%20lifespan.

[3] Electronic Medicines Compendium, "Summary of Product Characteristics Tostran 2% gel," Kyowa Kirin Ltd, Feb 2020. [Online]. Available: https://www.medicines.org.uk/emc/product/332/smpc#gref [Accessed Jan 2022].

[4] Somerset CCG, “Menopause and Hormone Replacement Therapy”, [Online]. Available: https://www.somersetccg.nhs.uk/prescribing-and-medicines-management/prescribing-guidelines-by-clinical-area/menopause-and-hormone-replacement-therapy/

[5] Electronic Medicines Compendium, "Summary of Product Characteristics Testogel 40.5mcg," Besins Healthcare (UK) Limited, Jun 2021. [Online]. Available: https://www.medicines.org.uk/emc/product/13255/smpc [Accessed Aug 2024].

[6] British Menopause Society, “Testosterone Replacement in Menopause”,[Dec 2022] https://thebms.org.uk/wp-content/uploads/2022/12/08-BMS-TfC-Testosterone-replacement-in-menopause-DEC2022-A.pdf [Accessed Aug 2024]

[7] Electronic Medicines Compendium, "Summary of Product Characteristics Testim," Endo Ventures Limited, Oct 2020. [Online]. Available: https://www.medicines.org.uk/emc/product/9633 [Accessed Jan 2022].