THE SHEFFIELD AREA PRESCRIBING GROUP

Shared Care Protocol

For

Topical testosterone replacement therapy in menopausal women

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Shared Care Protocol
Topical testosterone replacement therapy in menopausal women

Statement of Purpose

This shared care protocol (SCP) has been written to enable the continuation of care by primary care clinicians of women initiated on topical testosterone preparations for the management of menopausal symptoms by the menopause clinic at STHFT, where this is appropriate and in the patients' best interests. Use of testosterone in premenopausal women is not included in this SCP.

Treatment of menopausal women is an unlicensed indication and this SCP does **not** cover the licensed indication of adult male hypogonadism. Prescribers should note the GMC guidance 'Good practice in prescribing and managing medicines and devices' on shared care and prescribing unlicensed medicines.

This SCP does not preclude primary care prescribers from initiating testosterone without referral to the menopause clinic, provided they have the knowledge and competency to do so. For these prescribers, the SCP provides a prescribing guideline and the relevant requirements under responsibilities of the specialist and primary care clinician should be undertaken.

Responsibilities of specialist clinician

- To discuss benefits and side effects of treatment with the patient/carer and obtain informed consent, in line with national guidance; this is particularly important as the indication is unlicensed.
- To provide patient / carer with contact details for support and help if required.
- To direct the patient / carer to information sources (for details see Information for patients) including the Women's Health Concern testosterone replacement factsheet
- To advise the patient on administration and the precautions to reduce the risk of transfer through physical contact, in line with the MHRA Drug Safety Update. See additional information.
- To initiate topical testosterone replacement in appropriate patients.
- To monitor as detailed below.
- To prescribe the first month's supply and monitor until patient stable.
- To contact patient's primary care prescriber to request prescribing and, once stable, monitoring under shared care and send a link to or copy of the shared care protocol.
- To advise the primary care prescriber regarding dosage and continuation of treatment, including the duration of treatment.
- To discuss any concerns with the primary care prescriber regarding the patient's therapy.
- The patient to normally remain under the specialists' care, but if on-going specialist co-ordination of the patient's care is not required an individual care plan should be agreed on a case by case basis. This may include access to advice and intervention of the specialist in a timelier manner than via a new referral.

Responsibilities of the primary care clinician

- To refer appropriate patients to the menopause clinic for assessment.

- To contact the requesting specialist if concerns in joining in shared care arrangements; it will be presumed by the referring specialist that the primary care team is operating under this shared care protocol. Should the primary care prescriber feel unable to act under this shared care protocol they should discuss with the specialist requesting the care in the first instance. If, after discussion, they still feel unable to prescribe then the primary care clinician must notify the specialist in writing.
- To report any serious adverse reaction to the appropriate bodies e.g. MHRA and the referring specialist.
- To continue to prescribe for the patient as advised by the specialist.
- Ensure monitoring as indicated in monitoring section below.
- To inform the specialist if the patient discontinues treatment or monitoring for any reason.
- To seek the advice of the specialist if any concerns with the patient's therapy.
- To conduct an annual medication review or more frequent if required. To reinforce the advice to patients on administration, including the precautions to reduce the risk of transfer through physical contact, in line with the MHRA Drug Safety Update. See additional information.
- In the event that the primary care prescriber is not able to prescribe, or where the SCP is agreed but the specialist is still prescribing certain items e.g. hospital only product, the primary care prescriber will provide the specialist with full details of existing therapy promptly by a secure method on request.
- For medication supplied from another provider prescribers are advised to follow recommendations for Recording Specialist Issued Drugs on Clinical Practice Systems.

Responsibilities of Patients or Carers

- To be fully involved in, and in agreement with, the decision to move to shared care.
- To attend hospital and primary care clinic appointments (in person or by telephone) and to bring monitoring information e.g. blood test results (if required). Failure to attend will potentially result in the medication being stopped.
- Present rapidly to the primary care prescriber or specialist should the clinical condition significantly worsen.
- Report any suspected adverse effects to their specialist or primary care prescriber whilst taking testosterone.
- To read the information on the menopause and use of testosterone (for details see Information for patients).
- To apply the topical testosterone as prescribed.
- To follow the recommendations on safe administration, including the precautions to reduce the risk of transfer through physical contact.
- Inform the specialist, primary care prescriber or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication.

Indication

Testosterone replacement in menopausal women (medical or surgical or physiological menopause), who present with loss of libido on conventional hormone replacement therapy (HRT). Menopausal women includes women in perimenopause and postmenopause (see NICE NG23). There are very few data for testosterone replacement in premenopausal women which remains a controversial area requiring more research (BMS 2022).

Testosterone levels naturally decline through a woman's lifespan. Loss of testosterone is particularly marked after surgical or medical menopause. Testosterone contributes to libido, arousal and orgasm by increasing dopamine levels. Testosterone also maintains muscle and bone strength, cognition and mental well-being. Reduced testosterone levels may lead to

loss of libido, difficulties achieving orgasm, fatigue, loss of motivation. As RCTs of testosterone have not demonstrated beneficial effects on other symptoms, the primary indication for testosterone is loss of libido following a biopsychosocial approach (BMS 2022).

There are currently no licensed products for testosterone replacement in women in the UK.

Available preparations that may be used (out of licence/ 'off label') include: Testogel® gel sachet 40.5mg/2.5g; Testim® gel tube 50mg/5g; Testogel® pump dispenser 16.2mg/g; Tostran® 2% pump.
Note: AndroFeme (testosterone 1% cream) is licensed in Australia for female usage and may be imported to the UK for private prescribing under special MHRA licence. It is not included in this SCP.

National guidance:
NICE guidance NG23 www.nice.org.uk/guidance/ng23
British Menopause Society (BMS) – Testosterone replacement in menopause https://thebms.org.uk/publications/tools-for-clinicians/testosterone-replacement-in-menopause/

Selection of patients

Menopausal women with loss of libido on oestrogen containing HRT; testosterone may be used with or without systemic HRT, although the incidence of androgenic side-effects is likely to be higher in women not using oestrogen containing preparations. The urogenital tissues should be adequately oestrogenised in women with vulvovaginal atrophy / genitourinary syndrome of the menopause e.g. through use of vaginal oestrogen, to avoid dyspareunia.

Testosterone can be considered in women who are still experiencing low sexual desire despite HRT. However, there are many other psychosocial factors which can impact on sex drive, which should also be considered and excluded before referral to the menopause clinic.

Excluding patients – see contra-indications below:

Dosage

The starting dose is approximately 5mg per day; this can be delivered as follows:

Product	Testosterone content	Dose	Pack information
Testim 50mg transdermal gel *	50mg testosterone in 5g tube	1/10 tube (5mg testosterone) applied per day **Or** ¼ tube (12.5mg testosterone) applied on alternate days	One 5g tube provides 8-10 days supply.
Testogel 40.5mg transdermal gel in sachet *	40.5mg of testosterone per 2.5g sachet	1/8 sachet applied per day (approx. 5mg testosterone daily)	One 2.5g sachet provides 8 days supply.
Testogel 16.2 mg/g gel	16.2mg testosterone in 1g of gel.	1 metered dose/1 pump actuation (20mg testosterone) applied	One pump containing 88g of gel delivers a minimum

	One pump actuation delivers 1.25g of gel containing 20.25mg of testosterone.	twice weekly **or** ½ metered dose (10mg testosterone) applied 4 x per week.	of 60 pump actuations providing 210 days / 30 weeks (approx. 7 months) supply.
Tostran 2% Gel	20mg testosterone in 1g of gel One press of the canister piston delivers 0.5g of gel containing 10 mg testosterone.	1 metered dose/1 pump actuation (10mg testosterone) applied on alternate days	One container containing 60g of gel delivers approx. 120 pump actuations providing 240 days / 34 weeks (approx. 8 months) supply.

*Local preferred formulations as the pump preparations may lead to high testosterone levels and more side-effects

See also additional information

Duration of use should be individualised and benefits/risks evaluated at least on an annual basis.

Contra-indications

During pregnancy and breast feeding
Active liver disease
History of hormone sensitive breast cancer (exceptions may be made for those with intractable symptoms)
Competitive athletes
Women with upper normal or high baseline testosterone / free androgen index (FAI) levels
Women with hypersensitivity to active ingredients or excipients.

Side –effects

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 to treatment, the primary care clinician should contact the specialist for advice on reducing the dose or stopping the treatment.

- Increased body hair at the site of application - occasional problem - spread more thinly, rotate site of application, reduce dose
- Generalised hirsutism – uncommon - reduce dose/stop
- Alopecia, male pattern baldness, hair loss – uncommon – reduce dose/stop
- Acne, greasy skin – uncommon - reduce dose/stop
- Deepening of voice – rare - reduce dose/stop
- Enlargement of clitoris - rare – reduce dose stop

- Localised skin reactions

The long-term side effects of testosterone usage in women are unknown. However, RCTs and meta analyses have not shown an increased risk of cardiovascular disease or breast cancer but longer-term trials are needed.

Monitoring

Response to testosterone is highly variable due to varying absorption and metabolism. Side effects are uncommon when levels are kept in the female physiological range.
Note: Monitoring of total serum testosterone is undertaken not to diagnose a low testosterone level, but to establish a baseline, assess whether testosterone can be safely initiated and to ensure levels remain within the normal range for premenopausal women.

Specialist monitoring
Total serum testosterone to be measured prior to commencement of testosterone therapy and after 3 months of treatment. Repeat levels 2-3 monthly until stable. This will be organised and reviewed by the menopause clinic.

Monitor symptom relief – stop testosterone after 6 months if physiological levels have been raised within normal range, without improvement in symptoms.

Primary care clinician monitoring
Annual total serum testosterone when stable, symptom and side effect review for those who continue to use testosterone.

Ensure total serum testosterone remains within the normal physiological range for premenopausal women, using the local laboratory reference.

Abnormally raised total serum testosterone: if a single total serum testosterone is raised beyond the laboratory normal range for premenopausal women in the absence of symptoms, do not modify the dose; repeat the measurement, advising the patient not to apply testosterone prior to sampling; and contact the specialist with this result if it is also abnormal.

If appropriate report any serious adverse reaction to the MHRA, using the yellow card system.

Interactions

Please refer to the current BNF and the SPC.

Additional information

Apply testosterone with clean hands to clean, dry skin on lower abdomen or upper thighs.

Wash hands immediately after application

Do not cover skin for 3-5 minutes until dry.

Testogel® sachet – do not wash the site for 1 hour.
Testim® gel - do not wash site for at least 6 hours.
Testogel® pump dispenser - do not wash site for 2 hours.
Tostran® pump - do not wash site for at least 2 hours.

Avoid skin to skin contact with applications to prevent testosterone transfer to others, especially pregnant women and children.

The risk of transfer can be reduced by washing hands after application, covering the application site with clothes or by washing site with soap and water prior to contact. Washing the site should be after the recommended time period following application has passed to maximise the absorption in the patient. The MHRA has issued a Drug Safety Update (25 Jan 23) advising health care professionals to inform patients of the risk of transfer, the adverse effects that may occur and the precautions to be taken to minimise this.

Note
The HRT prepayment certificate, introduced on 1 April 2023, which saves money for those who pay 3 or more HRT prescription charges within 12 months, does not apply to transdermal testosterone products. It only applies to products licensed for HRT, see list here.

Re-Referral guidelines

Refer back to Dr Stillwell or referring specialist at the menopause clinic as needed: for symptom control, discussion re medication, side effects etc.

Contacts for Support, education and information

Dr Sue Stillwell
Menopause Lead
Jessop Wing
Royal Hallamshire Hospital
Sheffield

Secretary Lesley Mercer- Colposcopy office – Jessop wing
Tel 0114 2268300

Susanstillwell@nhs.net

www.thebms.org.uk British menopause society – Tools for clinicians testosterone replacement in menopause – information for GPs and other health professionals.
https://thebms.org.uk/publications/tools-for-clinicians/testosterone-replacement-in-menopause/

Information for patients:
https://www.womens-health-concern.org/ factsheets – testosterone for women
https://www.womens-health-concern.org/help-and-advice/factsheets/testosterone-for-women/

Rockmymenopause.com Rock My Menopause is a public campaign of the Primary Care Women's Health Forum (PCWHF)

Menopausedoctor.co.uk

Note: These sources are recommended to assist patients with their understanding and management of the menopause, HRT and use of testosterone. Neither the Sheffield APG nor STHFT is responsible for their content.

Equality and Diversity

The SCP is only applicable in the management of menopause and therefore only applies to ciswomen. There is a Sheffield pathway for testosterone replacement for men and a SYB ICS collaborative care protocol for transmen.

References

Achillli C et al. 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

Barber RJ, Panay N, Fenton A, International Menopause Society (IMS) writing group. 2016 IMS Recommendations on women's midlife health and hormone therapy.
Climacteric. 2016; 19(2):109-150

Islam RM et al. Safety and efficacy of testosterone for women: a systematic review and meta-analysis of RCT data.
Lancet 2019; 7 (10):754-766

NICE NG23: Menopause Diagnosis and management November 2015 updated December 2019
www.nice.org.uk/guidance/ng23

British Menopause Society (BMS) – Testosterone replacement in menopause updated Dec 2022
https://thebms.org.uk/publications/tools-for-clinicians/testosterone-replacement-in-menopause/

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

MHRA Drug Safety Update: Topical testosterone (Testogel): risk of harm to children following accidental exposure. 25 Jan 2023
https://www.gov.uk/drug-safety-update/topical-testosterone-testogel-risk-of-harm-to-children-following-accidental-exposure

NHS England Responsibility for prescribing between Primary & Secondary/Tertiary Care (January 2018)
https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

Full details of prescribing information on topical testosterone products is given in the manufacturers summary of product characteristics (SPCs), available from www.medicines.org.uk ; however, note these refer to the licensed use in male hypogonadism.

Version history

Version 2 has been updated from version 1, approved by APG July 2021, in line with the BMS update May 2022, further updated Dec 22, and the reformulated Testogel sachet presentation.

Version 2.1: Amendment to Additional Information and responsibilities of clinicians and patients following the MHRA Drug Safety Update (25 Jan 23) on the risk of transfer of topical testosterone and the precautions to be taken. Addition of note that the HRT pre-payment certificate does not apply to transdermal testosterone products

Acknowledgement: Dr Laura Cawley, Locum GP and accredited BMS menopause specialist