Bath and North East Somerset, Swindon and Wiltshire Together

SHARED CARE AGREEMENT
OFF-LABEL Topical Testosterone in adult women on HRT
Amber TLS – 3 Months

Principles of Shared Care

Shared care agreements provide a framework for the seamless transfer of care from a hospital or specialist service setting to general practice, where this is appropriate and, in the patient's best interest. When a specialist considers a patient's condition to be stable or predictable, they may seek the agreement of the GP (or other primary care prescriber) and the patient to share their care.

Patients and/or carers must be centrally involved in any decision-making process. They should be supported by good quality information that helps them to both come to an informed decision about engagement in a shared care arrangement and sets out the practical arrangements for ongoing supplies of medicines.

The existence of a shared care agreement does not necessarily mean that the GP has to agree to and accept clinical and legal responsibility for prescribing; they should only do so if they feel clinically confident in managing that condition. Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.

This SCA is used to facilitate the prescribing of the off-label use of testosterone in women as part of HRT for the treatment of low sexual desire.

***A specialist in menopause for the purposes of this SCA is**: a British Menopause Society accredited specialist or equivalent prescriber who can demonstrate that they have received training in and have clinical experience of treating women with testosterone preparations. This could therefore be a GP working in primary care.

Responsibilities of Secondary Care Menopause Specialist / Specialist in menopause*

Initial management

- Consider other causes of low sexual desire and treat as appropriate – Topical oestrogens for Genitourinary syndrome of menopause, Other medications eg SSRI, Psychosexual and relationship counselling. Ensure patient is on NON-oral oestrogen replacement at optimal doses.
- Confirm diagnosis and indication for topical testosterone in-line with this shared care agreement.
- Ensure a baseline hormone profile has been done pre-testosterone treatment. For the purposes of testosterone monitoring a hormone profile should include Total Testosterone, Sex Hormone Binding Globulin (SHBG), Free Androgen Index (FAI).
- Discuss the risks of treatment with the patient, including time to response and potential side-effects.
- Discuss how and when to take the treatment and the effects and benefits expected.
- Discuss the need for blood tests and the patient pathway under the shared care agreement including the patient's responsibilities.
- Inform patient that this an off-label use of testosterone. Informed consent should be documented.
- Review concurrent medications for potential interactions prior to initiation.
- Initiate treatment and prescribe for 3 months.
- Communicate details of treatment to GP in writing and ask the GP whether they are willing to take over prescribing immediately or once the patient is stable (once) there has been sufficient time to allow optimisation of treatment and demonstration by symptom control and blood tests that show that the patient's response is consistent.
- Report adverse events to the MHRA via the yellow card scheme
- Follow up of patients including clinical assessment and review of their response to treatment should occur at 3 months, six months and then annually. This may be done by the Secondary or Primary Care teams depending on the agreement of the primary care team and upon the complexity of the patient and their needs.
- When the patient is discharged with prescribing passed onto the GP, the consultant will provide access to Patient Initiated Follow Up (PIFU) for the next year.
- The GP will be provided with access to consultant advice & guidance if required via Cinapsis.
- Inform GP if patient does not attend scheduled clinic appointments.

Responsibilities of GP / Primary Care Prescriber

- Reply to the request to take over care, as soon as practicable, if they are **unable** to support shared care (in writing or via secure email).
- After discharge from secondary care be responsible for care and monitoring as long as the dose and FAI are stable.
- Prescribe testosterone at the dose recommended after discharge, as long as the dose and FAI are stable.

- The British Menopause Society recommend that hormone profile blood tests are performed at 3 months, 6 months and then annually, or as specified by the consultant and review as per section 4.
- Undertake clinical assessment and review patient's response to treatment as part of annual HRT review or as specified by consultant.
- Stop treatment where appropriate or adjust dose of testosterone if needed according to blood test results (see section 4).
- Refer back to specialist if symptoms are not controlled or levels are not within normal, despite dose adjustments.
- Review any new concurrent medications for potential interactions
- Report adverse events to the MHRA via the yellow card scheme

Responsibilities of Patient / Carer

- Report to the specialist or GP if they do not have a clear understanding of the treatment.
- Share any concerns in relation to treatment with the medicine.
- Report any adverse effects to the Specialist or GP whilst taking the medicine.
- Attend appointments at least annually for blood tests, clinical review and monitoring.

1. Summary of condition and treatment aims Include links to relevant clinical guidelines e.g. NICE	**Background** Testosterone therapy can be considered, as per NICE, in postmenopausal women who are distressed by decreased sexual interest and where there is no other identifiable cause (e.g. medications SSRIs, vulvo-vaginal atrophy, relationship or psychosexual factors), and where estrogen replacement therapy (ERT) alone has not been effective. There is currently no evidence base for the relief of symptoms other than decreased sexual desire but studies are on-going. ERT should be used first and dose titrated to resolve estrogen deficiency symptoms. Tibolone™ can be considered. Women should be moved to the transdermal route of administration of ERT prior to consideration for testosterone therapy. Testosterone will only very rarely be given in isolation without estrogen and these patients would stay under secondary / specialist care for the duration of treatment. **There is currently no licensed testosterone preparation available in the UK for women. There are preparations of different strengths that are licensed for use in men. Preparations of 1 -1.62% are preferred for off label use in women.** NICE have published Menopause Guidance and Management NG23 (2015) regarding altered sexual function[1] which states the following: 1.4.8 *Consider testosterone supplementation for menopausal women with low sexual desire if HRT alone is not effective.* However, it notes: "At the time of publication (November 2015), testosterone did not have a UK marketing authorisation for this indication in women. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. The British Menopause Society (BMS) guidance[2] (https://thebms.org.uk/publications/tools-for-clinicians/testosterone-replacement-in-menopause) also acknowledges that there are no commercially available products for testosterone replacement in women in the UK.
2. Details of medicine and indication Please state whether licensed or unlicensed (off-label) use. Note that shared care is generally unsuitable for off-label prescribing unless it is a widely recognised use (e.g. included in BNF)	**Efficacy & safety: evidence review** • NICE NG23 Menopause: diagnosis and management (Nov 2015) full guidance p97: 8.2.5.2.4 Comparison of testosterone verses no treatment/placebo. Results: Significant increase in frequency of satisfying sexual intercourse. • BMS Testosterone in women • BMS statement on safety of testosterone Potential Side effects – increased hair growth, acne, greasy skin Rare potential side effects – Alopecia, Voice deepening, Clitoromegaly **Risks vs benefits** Risk changes as patients age, they might e.g. gain weight or develop conditions such

<table>
<tr><td></td><td colspan="2">as diabetes, so it is important to re-evaluate the risks vs benefits of using testosterone annually.

Oral vs transdermal ERT
All oral estrogens (oral contraceptives and oral ERT) will result in an increase in SHBG which will bind testosterone and reduce bioavailability. Patients using oral estrogen should be changed to transdermal estrogen before being considered for testosterone therapy[4].

Exclusions from this SCA
• Use of testosterone without ERT
• Use in breast cancer patients.
• Transgender patients AFAB wishing to transition</td></tr>
<tr><td rowspan="4">3. Pharmaceutical aspects</td><td>Route of administration:</td><td>Topical</td></tr>
<tr><td>Formulation:</td><td>See below</td></tr>
<tr><td>Administration details:</td><td>See below</td></tr>
<tr><td>Other important information:</td><td>See below</td></tr>
<tr><td>4. Usual dose and frequency (including details of dose adjustments, e.g. in renal impairment) and duration of therapy
Transfer of monitoring and prescribing to Primary care is normally after the patient is on regular dose and with satisfactory investigation results. All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.</td><td colspan="2">Product choice[2,8]: Several topical testosterone products are included on BSW formulary; all are used outside their license (off-label) when prescribed for use in women. Topical testosterone should be prescribed by brand; strength and presentation varies. Preparations of 1 -1.62% are preferred for off label use in women.
Please note that in Dec 2023 Testim® was discontinued: Medicine Supply Notification: Testosterone (Testim®) 50mg/5g transdermal gel unit dose tubes - Community Pharmacy England (cpe.org.uk)

Treatment options (off-label) (also see tables 1-3 page 5):

Testogel® 1.62% or 40.5mg/2.5g gel in sachet.
Each sachet holds 2.5g gel containing 40.5mg testosterone.
Starting dose usually 1/8th of a sachet applied daily, equates to 5mg/day. One sachet to last 8 days, one box contains 30 x sachets - one box to last 240 days.

The following product is in a pump format and is used locally by some specialists*:
• Tostran® 2% (20mg/g) gel in a multi-dose pump action container. One metered pump of 0.5g=10mg therefore usually given on alternate days. One pump will last 240 days at this dosage.

NOTE: Higher strength pumps Testogel® 16.2mg/g (20.25mg) and Testavan® 2% (20mg in 1g) are also available but as they give a higher dose per actuation, they should only be used in the event of stock shortages of the above preferred products. Testavan is not used locally and further information on this product is not included in this document.
• Testogel® 16.2mg/g (20.25mg) of testosterone in each measure of 1.25g gel in a multi-dose pump action container. The pump contains 60 doses and the patient would be instructed to use one actuation every 3-4 days (equivalent to 2 pumps per week, applied on the same day as the HRT patch is changed). This gives them an equivalent dose of 5-7 mg per day. One pump will last approximately 210 days if used twice a week.

Dose range: 3-10mg/day (rarely over 7mg/day), or as advised by Specialist on case by case basis and individual circumstances. Dose titrated according to the balance between Total Testosterone, SHBG and FAI levels taking into account that physiological testosterone serum levels decrease with increasing age. Younger women needing hormone replacement and other specific groups of women may need</td></tr>
</table>

higher doses of HRT. In general doses outside the normal recommended prescribing range should be advised by the Specialist and not initiated by the GP.

Application technique for the recommended products: The gel should be applied daily (or less often as advised by specialist if higher strength pump product is used, see above*) in the morning, and spread (without rubbing) over dry, intact skin on the lower abdomen or upper thighs, Allow 3 - 5 minutes to dry before dressing. Wash hands with soap and water after applications. The application site should be rotated to minimise application site reactions.

Testosterone Dosing Guide

Start treatment if Total testosterone (<1nmol/l) and FAI (<2%) are in the lower third of the female range. Testosterone treatment will usually be initiated at a dose of 5mg per day. The dose can then be increased or decreased depending on the interim blood test results.

Please note that as there are no licensed testosterone products available for use in women, the doses/frequencies in the tables below have been suggested by the local specialists.

Table 1: Testogel 40.5mg in 2.5mg sachets, 1.62% testosterone

	High		**Standard**		**Low**
Sachet to last	4 days	6 days	8 days	11 days	16 days
Dose	10mg	7mg	5mg	3.7mg	2.5mg
Number of sachets (available in box of 30)					
2 months	15	10	8	6	4
4 months	30	20	15	11	8
6 months	46	31	23	17	11

Higher strength products:

Table 2: Tostran ® 2% (20mg/g) gel in a 60g pump. One metered pump of 0.5g=10mg

	High	**Standard**	**Low**
Dose	10mg	5mg	2.5mg
Directions	1 pump OD	1 pump alt die	1 pump every 4th day
Pump will last	120 days	240 days	480 days

Table 3: Testogel® 16.2mg/g (20.25mg) of testosterone in each measure of 1.25g gel in a pump container.

	High	**Standard**	**Low**
Dose	10mg	5mg	2.5mg
Directions	1 pump OD	1 pump alt die	As per specialist recommendation
Pump will last	120 days	240 days	

Duration of use and review: The BMS[2] advise 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.
Women should be made aware prior to initiating testosterone treatment of the lack of long-term clinical trial safety data beyond 24 months associated with use of testosterone in physiological doses in women. Treatment should include regular monitoring and it should be an informed decision between physician and patient if treatment is to be continued beyond 24 months.[4]

Local specialists advise that there is no particular time limit for the use of testosterone. Testosterone can be used as long as a woman is on ERT and should be stopped when ERT is stopped and should only be used alone without oestrogen in exceptional circumstances (specialist recommendation only).

5. Baseline investigations and initial monitoring to be undertaken

Baseline investigations

- Baseline blood tests to be taken before starting testosterone replacement therapy: Total testosterone, SHBG and FAI.
- Assessment of blood pressure and BMI (primary care data can be used)

The BMS advise that testosterone assays can be performed to support a diagnosis of Female Androgen Deficiency Syndrome (FADS) also referred to as Hyposexual Sexual Desire Disorder. They recommend that the gold standard would be to measure free testosterone, however a calculation can be performed to work out the FAI which is used in practice. FAI monitoring can be useful for determining appropriateness of testosterone initiation, response to treatment and maintaining levels in normal range and thus reducing risk of hormonal side effects.

Women with a SHBG level above 160nmol/l are unlikely to benefit from testosterone therapy.[4] Although it is not mandatory to perform testosterone level estimation prior to or for monitoring treatment, it is useful and is recommended in the global consensus statement[5]. A low FAI < 2.0% in women with symptoms of low sexual desire, supports the use of testosterone supplementation. Repeat estimation at the 3 month follow up visit should be performed to demonstrate if there has been an increase in levels, though clinical response is of paramount importance. It is also useful to demonstrate that values are being maintained within the female physiological range, typically < 3-6% (4-9% for RUH lab), thus making androgenic side effects less likely.[2,6,7]

Guide to blood test results

The amount of each hormone needed is very dependent on age and circumstance. Younger women will usually need substantially more HRT. This is a rough guide only for women in their 50s.

Table 3:

	Low	**Medium**	**High***
Total testosterone nmol/l	<1	1-2	>2 (<2.7nmol/l for RUH lab)
SHBG nmol/l	0-40	40-120	>120[t]
Free androgen index %	<2.9	3-5.9	>6 (9% for RUH lab)
Interpretation of results	Start or increase treatment	No treatment or maintain current treatment	No treatment or reduce current treatment

- [t]Order LFT, TFT, prolactin and if any concerns discuss with a specialist.
- Take blood samples at the right timing according to the product used to avoid contamination of sample.
-

***If TT is > 2.0 (2.7 for RUH lab) OR FAI is >6%,**

1 Discuss with patient how they are using gel. Could there be contamination of blood sample?
2 Discuss with patient how they are feeling, symptoms / side effects?
3 Consider decrease dose of testosterone gel to next dosing point
4 Re-test blood after 3 months

If TT is < 1.0 or FAI is <2%

1 Discuss with patient how they are using the gel
2 Discuss with patient how they are feeling – symptoms / side effects?
2 Consider increase dose of testosterone to next dosing point
3 Re-test blood after 3 months

<table>
<tr><td></td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td></td><td>• Clinical response to treatment
• TT SHBG FAI</td><td>• Pretreatment
• At 3 months, at 6 months and then annually if stable</td></tr>
<tr><td>6. Ongoing monitoring requirements to be undertaken by primary care</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td></td><td>• Clinical response to treatment
• TT SHBG FAI</td><td>• Annually as part of HRT review</td></tr>
<tr><td>7. Action(s) to be taken by primary care if abnormal result(s)</td><td colspan="2">• Consider dose adjustment as per section 4, tables 1-3 above
• Discuss abnormal test results with the Specialist</td></tr>
<tr><td>8. Cautions and contraindications
Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.</td><td colspan="2">Cautions
• 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.
• Caution in renal impairment, nephrotic syndrome,
• Caution 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 / hypercalcuria developing from androgen therapy.
• Epilepsy and migraine (conditions may be aggravated)
• Thrombophilia; some reports of thrombotic events
• Testosterone may cause a rise in blood pressure
• History of liver tumours - only use cautiously with specialist involvement
• Limited experience of the use of testosterone in patients over 65 years of age. Currently, there is no consensus about age specific testosterone reference values.
• Competitive athletes
• Women with upper normal or high baseline total and FAI
Contraindications[4]
• Pregnancy and breastfeeding
• In cases of known or suspected hormone sensitive cancers e.g. breast carcinoma, androgen-dependent neoplasia, except with specialist advice. Off label exceptions to this may be agreed in fully informed women with intractable symptoms not responding to alternatives
• Known hypersensitivity to the active substance or any of the excipients.</td></tr>
<tr><td>9. Significant medicine and food interactions and management
For a comprehensive list, consult the BNF or Summary of Product Characteristics (SPC)</td><td colspan="2"><table>
<tr><td>Oral anticoagulants</td><td>Increased monitoring of international normalised ratio (INR) recommended particularly when started or stopped.</td></tr>
<tr><td>Corticosteroids</td><td>Increased risk of developing oedema. Co-administer with caution.</td></tr>
<tr><td>Insulin</td><td>Improved insulin sensitivity may occur in patients treated with androgens who achieve normal testosterone plasma concentrations following replacement therapy.</td></tr>
</table></td></tr>
<tr><td>10. Adverse effects and management
Include details of incidence, identification, importance and management.</td><td>Adverse Effect</td><td>Action to be taken if detected</td></tr>
<tr><td></td><td>• Most common (10%) were skin reactions. See SPC for the full list of side effects[8].
• Symptoms of androgen excess, such as hirsutism and acne, weight gain, are common with testosterone therapy, usually mild.</td><td>• If severe, contact specialist for further advice.</td></tr>
</table>

11. Advice to patients and carers The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.	• Ensure that the patient understands that there are no licensed products available in the UK for this indication and so prescribing is off-label. Clearly document this discussion • Close skin contact with the area of application within an hour of application, by a partner or children should be avoided. This may result in the partner or child absorbing some testosterone through the skin contact. Cover the application area with clothing once applied. • Testosterone for women. Womens Health Concern. Feb 2022 https://www.womens-health-concern.org/help-and-advice/factsheets/testosterone-for-women/ • Report any of the following side-effects: ○ Irritability/nervousness/weight gain ○ Nausea/vomiting, changes in skin colour or ankle swelling ○ Breathing disturbances, including those associated with sleep ○ Severe skin application site reaction	
12. Pregnancy and breast feeding	• It is the responsibility of all clinicians to provide advice on the need for contraception to patients on initiation and at each review. • Topical testosterone is contra-indicated for pregnant or breastfeeding women. No studies on women have been carried out. Pregnant women should avoid all contact with skin treated with testosterone. Testosterone can give rise to adverse, virilising effects on the fetus. In the event of contact with treated skin, the area should be washed with soap and water as soon as possible.	
13.	GWH	gwh.obstetricsandgynaecologyadvice@nhs.net or cinapsis if available
	RUH	ruh-tr.Gynaecology@nhs.net or cinapsis
	SFT	Cinapsis
14. Additional information	• There is no available data to support or not support use of testosterone in **pre-**menopausal women, to treat depression, bone loss or to prevent cognitive decline. • Testosterone should not usually be used alone • Testosterone should not be used alone or in combination with estrogens in Breast cancer patients	

15. References	1.) NICE Menopause Guidance and Management NG23 (2015) Altered sexual function. https://www.nice.org.uk/guidance/ng23/resources/menopause-diagnosis-and-management-pdf-1837330217413 2.) The British Menopause Society Tool for Clinicians; Testosterone replacement in menopause Feb 2019 https://thebms.org.uk/wp-content/uploads/2019/03/08-BMS-ToolforClinician-Testosterone-replacement-in-menopause-02D.pdf 3.) RM Islam, RJ Bell, S Green, M Page, S Davis. Safety and efficacy of testosterone for women: a systemic review and meta-analysis of randomised controlled trial data. Lancet Diabetes Endocrinol Jul 25 2019. https://www.thelancet.com/journals/landia/article/PIIS2213-8587(19)30189-5/fulltext 4.) Androfeme Summary of product characteristics ANDROFEME 1 Product Information (myhealthbox.eu) (Accessed 10/05/2022. Last Revised 23/211/2020) 5.) Global consensus position statement on the use of testosterone therapy for women. Davis S R et al. J Clin Endocrinol Metab 104: 4660–4666, 2019 6.) Testosterone therapy for menopausal women. Drug Ther Bull. 2017 May;55(5):57–60. Available at http://www.dtb.bmj.com 7.) British Society for Sexual Medicine. Guidelines on the management of sexual problems in women: the role of androgens (2010). Available from: https://www.bashhguidelines.org/media/1096/3117.pdf 8.) Summary of Product Characteristics for (Tostran 2% ; Testogel 40.5mg/g gels) via https://www.medicines.org.uk/emc
9.) To be read in conjunction with the following documents	• NHS England: Responsibility for Prescribing Between Primary & Secondary/ Tertiary Care. Ref 07573, Version 1.0, Published January 2018. Accessed via: https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/ • BSWPartnership: Guidance for prescribers when patients access both NHS and private services. Adopted for BSW April 2022. Accessed via: https://bswpartnership.nhs.uk/medicines/wp-content/uploads/sites/3/2022/02/Private-Treatments-BSW-guidance-.pdf
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Contributors	RUH/GWH/SFT obs/gynae teams
Date Last Updated	October 2022: Minor update to add specialist in menopause plus definition on p1. Updated note on managing the newly launched Testogel preparation. Formatting. January 2023: Clarification of which products should be used in women, strengths of the products and baseline investigations and thresholds. June/July 2023 – move annual review to primary care, after longer surveillance period by specialist and removal of FBC/oestradiol monitoring & updated ref ranges for RUH lab. Dec 23: Removal of discontinued product Testim, addition of dosage tables and review of patient pathway in secondary & primary care. April 25: FAI value ranges in table 3 updated.
Date First Approved by BSW	19/8/21
Review Date	December 25
Document Version	V3.1

Bath and North East Somerset, Swindon and Wiltshire Together

BSW Pathway for using testosterone in women for low sexual desire

Specialist assessment and recommends treatment. Informed consent required for off-label use.

Do not consider testosterone replacement for androgen deficiency, cognitive dysfunction, bone health, well-being or cardiovascular/metabolic benefits.

1 2

Measure baseline:

- FAI (Testosterone and SHBG, FAI <2% supports testosterone use; do not prescribe if >6%*)
- BP
- BMI

Contra-indications to Testosterone replacement:

- In cases of known or suspected breast carcinoma, known or suspected androgen-dependent neoplasia, nephrotic syndrome, history of thromboembolism or hypercalcaemia
- In cases of known hypersensitivity to the active substance or any of the excipients.
- Pregnancy & breastfeeding
- High total testosterone >2nmol/l OR High FAI >6%* (>9% for RUH lab)

3

Review at 3 and 6 months

- FAI (reduce dose if FAI>6%*) (9% for RUH lab)
- Stop if no clinical response
- If good response and FAI 2-6%* (9% for RUH lab) continue
- Agree monitoring schedule, target FAI, and how to obtain advice/support
- Monitor for signs & symptoms of androgen excess (hirsutism, acne, alopecia, voice deepening)

Testosterone therapy for postmenopausal women, in doses that approximate physiological testosterone concentrations for pre-menopausal women, is not associated with serious adverse events (Level I, Grade A).

Caution

Cardiac/hepatic/renal insufficiency; Migraine; Epilepsy; Diabetes Mellitus; IHD; Polycythaemia; Elderly; HTN; Competitive athletes; may potentiate sleep apnoea in some patients, especially those with risk factors such as obesity or chronic lung disease.

4

Review annually thereafter

- Topical testosterone should be stopped when ERT is stopped or if the specialist advises for it to stop.