GP Fact Sheet – Testosterone gel for women in the menopause

Background

Testosterone gel (Testim®/Testogel®/Tostran®) is recommended for restricted use for women in the menopause with Hypoactive Sexual Desire Disorder (HSDD) / Female Androgen Deficiency Syndrome (FADS) if Hormone Replacement Therapy (HRT) alone is not effective. Recommend as **AMBER INITIATION** – i.e**. GPs may continue therapy after initiation and stabilisation (3-6 months)** by a clinician with expertise in the treatment of the menopause (defined as a Consultant Endocrinologist/Gynaecologist or a primary care clinician who has relevant experience and is clinically competent to prescribe).

Further information relating to the use of testosterone gel for women in the menopause can be accessed from the British Menopause Society (BMS) Tool for Clinicians.[1]

A local **Patient Information Leaflet** – Testosterone gel for women in the menopause can be found here: HWE ICB patient information leaflet

Medicine	**Generic and Brand name:** Testosterone gel (Testim® or Testogel® or Tostran®)
Strength and formulation	Testim® testosterone 50mg/5g gel tubes Testogel® testosterone 50mg/5g gel sachets (***due to be discontinued by manufacturer March 2022, after which 40.5mg/2.5g sachets will be available***) Tostran® testosterone 2% gel pump dispenser containing 60g Following discontinuation of Testogel® 50mg/5g sachets (in March 2022), **the first choice product within Hertfordshire is Testim® 50mg/5g gel tubes**. Testogel® 40.5mg/2.5g gel sachets or Tostran® 2% gel pump dispenser may be prescribed where there are specific circumstances (e.g. supply problems, or to permit transfer of prescribing for patients successfully initiated on these products at specialist clinics).
Intended indication	Hypoactive Sexual Desire Disorder (HSDD) / Female Androgen Deficiency Syndrome (FADS) - **NB this is an 'off-label' use of testosterone gel.** For use as outlined in NICE Guideline 23 – Menopause: diagnosis and management:[2] **Altered sexual function** 1.4.8 Consider testosterone supplementation for menopausal women with low sexual desire if HRT alone is not effective. NICE CKS also states:[3] **If a woman has menopausal symptoms, consider arranging referral to a healthcare professional with expertise in menopause if:** The women has persistent altered sexual function and hormonal and/or non-hormonal, or non-drug treatments are ineffective: • Seek specialist advice regarding the use of testosterone supplementation (off-label use) • Consider referral for psychosexual counselling, depending on the woman's wishes
Safety[1]	Response to testosterone with regards to efficacy and adverse effects, is highly variable. This is most likely due to varying absorption, metabolism and sensitivity to testosterone. 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, the dosage should be reduced, or treatment stopped. • 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) Randomised controlled trials and meta analyses have not shown an increased risk of cardiovascular disease or breast cancer although longer term trials would be desirable.
When should testosterone be avoided or used with caution? [1]	• During pregnancy or breastfeeding • Active liver disease • History of hormone sensitive breast cancer – off-label exceptions to this may be agreed in fully informed women with intractable symptoms not responding to alternatives • Competitive athletes – care must be taken to maintain levels well within the female physiological range • Women with upper normal or high baseline testosterone levels / Free Androgen Index (FAI)
Dose and administration	**For Adults** While unlicensed for use in women, the British Menopause Society recommend the use of either Testim®, Testogel® or Tostran®:[1] • Testim [Endo Ventures Ltd] (1% testosterone gel in 5g tubes containing 50mg testosterone): Starting dose 1/10 of a tube/day = 5mg/day i.e. each tube should last 10 days. The amount to apply each day is approximately equal to the size of the tip of a ballpoint pen lid (such as a Biro). The tube should be kept in the fridge between uses. • **Due to be discontinued from March 2022:** Testogel [Besins Healthcare UK] (1% testosterone gel in 5g sachets containing 50mg testosterone): Starting dose 1/10 of a sachet/day = 5mg/day i.e. each sachet should last 10 days. The amount to apply each day is approximately equal to the size of the tip of a ballpoint pen lid (such as a Biro). The sachet should be kept in the fridge between uses. • **Introduced to market 2022:** Testogel [Besins Healthcare UK] (2% testosterone gel in 2.5g sachets containing 40.5mg testosterone): Starting dose 1/8 of a sachet/day = 5mg/day i.e. each sachet should last 8 days. The sachet should be kept in the fridge between uses. **NB this is double the potency of the Testogel 50mg/5g sachets, therefore the volume applied per day is proportionately less.** • Tostran [Kyowa Kirin Ltd] (2% testosterone gel in a canister containing 60g): Starting dose 1 metered pump of 0.5g = 10mg on alternate days. The testosterone gel should be to applied to clean dry skin (lower abdomen/upper thighs) and allowed to dry before dressing. 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. *When treating low sexual desire/arousal it is also important that urogenital tissues are adequately oestrogenised in women with vulvovaginal atrophy / genitourinary syndrome of the menopause e.g. through use of vaginal oestrogen, to avoid dyspareunia.*
Maximum quantity to be prescribed	Based on the above dosage recommendations: • Testim® (1% testosterone gel in 5g tubes containing 50mg testosterone): **30 x 5g tubes should last 300 days** • Testogel® (1% testosterone gel in 5g sachets containing 50mg testosterone): **30 x 5g unit dose sachets should last 300 days** • Testogel® (2% testosterone gel in 2.5g sachets containing 40.5mg testosterone): **30 x 2.5g unit dose sachets should last 240 days** • Tostran® (2% testosterone gel in a canister containing 60g): **each canister should last 240 days**
Patient monitoring & duration of use	NICE Guideline [NG23] recommends that each treatment for short-term menopausal symptoms should be reviewed:[2] • At 3 months to assess efficacy and tolerability (to be carried out by initiating clinician) • Annually thereafter unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side-effects or adverse events) The British Menopause Society recommends a 3-6 month trial of testosterone therapy before being discontinued due to lack of efficacy. 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.[1] It is estimated that women will remain on treatment for approximately 5 years.
Blood Test Monitoring	Its recommended that total testosterone, sex hormone binding globulin (SHBG) tests and Free Androgen Index (FAI) estimates should be done **prior to starting treatment, then at 3 and 6 months post starting therapy, then annually**, with blood tests performed sooner if patients have symptoms. Although it is not mandatory to perform testosterone level estimation prior to treatment, a low FAI < 1% in women with symptoms of low sexual desire and arousal, supports the use of testosterone supplementation. Repeat estimation at the 2-3 month follow up visit can be performed to demonstrate if there has been an increase in levels, though clinical response is of paramount importance.[1] Ongoing blood test monitoring is needed to demonstrate that values are being maintained within the female physiological range, typically a FAI < 5%, thus making androgenic side effects less likely.[1] If results are above the female physiological range, the dosage of testosterone gel should be reduced, or treatment stopped. Advice should be sought from the initiating specialist if required. If patients experience androgenic adverse effects (as listed above), blood monitoring should be performed. Where results are above the female physiological range, actions should be taken as above.

	The HWE ICB testosterone Patient Information Leaflet advises that patients keep a record of when their next blood test is due so that they can work together with their GP to make sure the tests are done at the right time.
Availability of blood test monitoring	Testosterone assays are available to GPs locally as follows: • WHHT – total testosterone and SHBG tests are available. If SHBG is requested, then FAI is also available. NB – WHHT have asked that testosterone assays in women are annotated to advise that the patient is receiving testosterone replacement to prevent labs confirming the result against another more expensive method (due to the specificity of the current method used). • ENHT – total testosterone & SHBG available – system does not currently calculate FAI, but this can be calculated as follows: FAI = Total Testosterone x 100 / SHBG.
Prescribing and monitoring responsibilities	As patient assessment and selection is key, treatment should be initiated and stabilised by an expert in the treatment of the menopause (defined as a Consultant Endocrinologist/Gynaecologist or a primary care clinician who has relevant experience and is clinically competent to prescribe). GP to continue therapy after the patient is stabilised on therapy, typically after a 3-6 month trial, and conduct the patient annual review (unless there are clinical indications for an earlier review). All blood test monitoring (see above) will be undertaken by the clinician who is prescribing for the patient. The initiating clinician will therefore carry out the baseline and at least the 3 month monitoring. Once the patient is stabilised on treatment, the initiating clinician will hand over prescribing and monitoring responsibility to the GP, with clear instructions about when/what tests are required.
Criteria for seeking further advice/referral	The following are examples: • Adverse Drug Reaction • Advice on blood test monitoring • Diagnosis of new complex medical conditions
Private to NHS Care	After recommendations from a private consultant/specialist, GPs should only take on prescribing of testosterone gel for women in the menopause if the patient's clinical circumstances meet the initiation criteria set out in NICE guideline [NG23][2] and this bulletin. GPs should also be sure that the private consultant/specialist has expertise in managing the menopause and is following the prescribing and monitoring responsibilities set out in this bulletin. As with all recommendations to prescribe from a private consultant/specialist, GPs do also not have to take on prescribing if in the exercise of their clinical discretion they do not think it is medically appropriate for the patient, the testosterone preparation is not listed on the HWE formulary, or they are unwilling to accept clinical responsibility for prescribing the medication.
References / Further reading	1. British Menopause Society. Tools for Clinicians – Testosterone replacement in menopause. Published May 2022. Available at: https://thebms.org.uk/publications/tools-for-clinicians/testosterone-replacement-in-menopause/ 2. National Institute for Health & Care Excellence. Menopause: diagnosis and management [NG23]. Available at: https://www.nice.org.uk/guidance/ng23 3. NICE Clinical Knowledge Summaries > Menopause > Management. Available at: https://cks.nice.org.uk/topics/menopause/management/management-of-menopause-perimenopause-or-premature-ovarian-insufficiency/

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Adapted from Bedfordshire, Luton and Milton Keynes ICS fact sheet: Testosterone Gel for low sexual desire in post-menopausal women.

Version	V2.2 Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include: • Rebadging with HWE ICB and removal of WECCG, ENHCCG and HVCCG headers and references • Review date removed and replaced with standard statement.
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