North Central London
Joint Formulary Committee

Factsheet

TESTOSTERONE GEL (Tostran® or Testim®)

Low sexual desire in menopausal women or women with premature ovarian insufficiency

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Document Control		
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Disclaimer
Factsheets support GPs in taking ongoing responsibility for continuing a medicine initiated in secondary care. It differs from a shared care agreement where secondary cares retain a proportion of responsibility for ongoing care.

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Factsheet – TESTOSTERONE GEL (Tostran® or Testim®) for low sexual desire in menopausal women or women with premature ovarian insufficiency

Indication information

As per local formulary agreement, testosterone gel (Tostran® or Testim®) is recommended for restricted use for low sexual desire in menopausal women or women with premature ovarian insufficiency, who had no improvement with oestrogen-based HRT alone. The definition of menopausal includes medical and surgical menopause. This is an 'off-label' use of testosterone gel.

Treatment should be initiated by a clinician with expertise in the treatment of the menopause who will consider contraindications and cautions for use.

The hospital team will:

1. Provide the patient with initial information regarding the treatment and possible adverse effects
2. Initiate and optimise (stabilise) treatment and inform GP when patient is stable on dose so that GP can continue prescribing (typically after 3 months).
3. Change dose if necessary and inform patient and GP of dose changes.

Dose and Administration

Testosterone gel are licensed for male hypogonadism; use in women is off-label and requires a lower dose (see table) and should be initiated by a clinician with expertise in the treatment of the menopause.

	Tostran 2% gel **[Kyowa Kirin Ltd]** 2% testosterone gel in a canister containing 60g	**Testim 50mg/5g gel** **[Endo Ventures Limited]** 5g tube of 50 mg testosterone
Starting dose	10mg (1 press of canister) on alternate mornings	5mg ($^1/_{10}$ of a tube[†]) each morning *i.e. 1 tube lasts 10 days*
Maximum dose **(see Clinical Monitoring)**	10mg (1 press of canister) alternating with 5mg (½ press of canister) each morning	7.5mg ($^1/_7$ of a tube) each morning *i.e. 1 tube lasts 7 days*
Application instructions	Apply to clean, dry, intact skin over abdomen or inner thigh (rotate sites daily to reduce irritation). Rub until dry. Wash hands with soap and water.	Apply to clean, dry, intact, skin of the shoulders and/or upper arms. Rub until dry. Wash hands with soap and water.
Prescribing quantities	If 10mg on alternate mornings: - 1 canister every 8 months If 10mg alternating with 5mg each morning: - 1 canister every 5 months	If 5mg each morning: - 3 tubes per month If 7.5mg each morning: - 5 tubes per month

[†] 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 a clean container and store it in a cool dry place (i.e. a cupboard away from direct sunlight) between uses.

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 low sexual desire from oral to transdermal oestrogen can be beneficial as this can increase the proportion of circulating free testosterone without requiring exogenous testosterone, though is not considered a mandatory step before offering testosterone gel. It is important that any symptoms of vulvovaginal atrophy are also adequately treated if testosterone is being considered for HSDD. Although studies have shown that testosterone can be beneficial in women not using concomitant oestrogen containing hormone therapy, the incidence of adverse androgenic effects such as acne and excess hair growth is higher; this strategy is therefore not usually recommended in routine clinical practice.

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'.

***Renal impairment**:* If severe renal impairment discontinue treatment

***Hepatic impairment**:* If severe hepatic impairment discontinue treatment

Adverse Effects

Adverse effects of testosterone in women are uncommon if levels are maintained within the female physiological range; see Clinical Monitoring section.

Adverse effect	Frequency	Suggested management by GP
Increased body hair at site of application	Occasional	Spread more thinly, vary site of application, reduce dosage
Irritation	Occasional	Rotate administration site; usually reduces over time. If there is severe application site reaction, treatment should be reviewed and discontinued if necessary.
Generalised hirsutism	Uncommon	Consider reduction in dosage
Alopecia, male pattern hair loss	Rare	Consider reduction in dosage
Acne and greasy skin	Uncommon	Consider reduction in dosage Can use topical measures to reduce acne if tolerated
Deepening of voice	Rare	Consider reduction in dosage or stopping
Enlarged clitoris	Rare	Consider reduction in dosage or stopping
Weight gain	Occasional	Consider reduction in dosage or stopping

Contraindications

- 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
- Avoid in patients with a known or suspected carcinoma of the breast
- Caution in patients with epilepsy and migraine as these conditions may be aggravated
- Hypersensitivity to active ingredients or excipients

Special Warnings and Precautions for Use

- 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. Testosterone may give positive results in a doping test.
- Women with upper normal or high baseline testosterone levels / FAI
- Avoid skin to skin contact with applications to prevent testosterone transfer to others, especially pregnant women and children
    - Inform patients of the possible effects of accidental exposure in women (e.g., facial and/or body hair growth, deepening of voice & changes in menstrual cycle) or in children (genital enlargement, premature puberty, development of pubic hair)
    - Counsel patients on methods to reduce risk of accidental exposure including washing hands with soap and water after application.
    - Further information can be found in the MHRA Drug Safety Update

Drug Interactions

When androgens are given simultaneously with anticoagulants, the anticoagulant effect can increase. Patients receiving oral anticoagulants require close monitoring of their INR especially when the androgen treatment is started, stopped or the dose of testosterone gel changed.

The concurrent administration of testosterone with corticosteroids may increase the likelihood of oedema; thus, these drugs should be administered with caution, particularly in patients with cardiac, renal or hepatic disease.

Clinical Monitoring

NICE Guideline [NG23] recommends that each treatment for short-term menopausal symptoms should be reviewed

Test	Frequency	Action if out of range
Efficacy and tolerability	After 3 months, then annually	At 3-4 month review (hospital): Adjust dose as necessary At annual review (GP): Dose to be titrated to, or discontinued, informed by FAI (see below). Discontinue if no benefit.
Free Androgen Index (FAI) estimates **Or** Total testosterone	Baseline, after 3 months, then annually	At 3-4 month review (hospital): Adjust dose as necessary, though clinical response is of paramount importance. At annual review (GP): Ongoing blood test monitoring is needed to demonstrate that values are being maintained within the female physiological range, typically a FAI < 5% or total testosterone level not exceeding upper limit of normal postmenopausal range (usually 2 nmol/L), thus making androgenic side effects less likely. 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.

GPs should review their patients as per their normal practice. Any suspected adverse reactions should be reported using the Yellow Card Scheme.

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Additional resources

A 'Testosterone for women' patient information leaflet is available from Women's Health Concern 'Factsheet'[1]

References

1. Tostran 2% Gel SmPC (2019). https://www.medicines.org.uk/emc/product/332 (accessed December 2022)
2. Testim SmPC (2022). https://www.medicines.org.uk/emc/product/9633/ (accessed December 2022)
3. NCL Joint Formulary Committee. Meeting minutes April 2016. https://www.ncl-mon.nhs.uk/wp-content/uploads/JFC/Minutes/1604_NCL_JFC_Minutes_April2016.pdf (accessed December 2022)
4. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press https://bnf.nice.org.uk/drugs/testosterone/ (accessed December 2022)
5. https://bnf.nice.org.uk/drug/testosterone.html#indicationsAndDoses
6. British Menopause Society. Testosterone replacement in menopause 'Tool for Clinicians' (2022). https://thebms.org.uk/publications/tools-for-clinicians/testosterone-replacement-in-menopause/ (accessed December 2022)
7. NICE NG23 Menopause: diagnosis and management (2019). https://www.nice.org.uk/guidance/ng23/chapter/ecommendations (accessed December 2022)

[1] The 2022 version of this leaflet is confirmed as being appropriate for NHS use