North Yorkshire & York Area Prescribing Committee

Topical testosterone for management of Low libido in menopausal and post-menopausal women

Traffic light classification - Green

Information sheet for Primary Care Prescribers

Indication: Management of Low Libido in Menopausal (both natural and surgical) and postmenopausal women

Therapeutic Summary:

The role of androgens in maintaining well-being in women is not fully understood. Testosterone is an important female hormone. Healthy young women produce approximately 100 – 400 mcg per day. Between a women's mid 30's and early 60's, adrenal androgen production reduces by about two-thirds. After a natural menopause, ovarian production continues to a varying degree. After bilateral oophorectomy, ovarian production of androgens and precursor sex hormones is lost. It has been suggested that there is a link between low circulating concentrations of testosterone and reduced sexual functioning in postmenopausal women.

In postmenopausal women who are distressed by low libido and who have no other identifiable cause (e.g. physical and psychosocial factors and medications), testosterone therapy if HRT alone is not effective can be considered. National institute for Health and Care Excellence (NICE) Guideline NG23 Menopause: diagnosis and management states - Consider testosterone supplementation for menopausal women with low sexual desire if HRT alone is not effective. The British Menopause Society (BMS), A new tool for clinicians: Testosterone replacement in menopause states, the loss of sexual desire is complex and may have hormonal, medical, psychosexual and psychosocial aetiologies. In clinical trials of women with low libido, approximately 2/3 of women responded positively to testosterone therapy (compared to 1/3 using placebo). The trials demonstrated that response may not be immediate, taking 8-12 weeks in some instances for the effect to become clinically significant.

Before initiating the treatment

- Investigate other causes of low libido, these include physical and psychosocial factors and medications, and HRT alone is not effective.
- Carry out blood tests to check sex hormone binding globulin (SHBG) and testosterone to show that FAI (free androgen index) is within the normal range before treatment is started.
  Reference range for Females 20 - 49 years: 0.3 - 5.6%
  >50 years: 0.2 - 3.6%
  Note women with a SHBG (Sex Hormone Binding Globulin) level above 160nmol/l are unlikely to benefit from testosterone therapy
- Ensure that women are on HRT before and while taking testosterone.

Testosterone Treatment

- Tostran® [Kyowa Kirin Ltd] (2% testosterone gel in a canister containing 60g) is the product of choice.

Dosage and route of administration

- Starting dose 1 metered pump of 0.5g of gel = 10 mg of testosterone twice a week (each canister should last 120 doses). This can be increased to three times a week if required.
  Patients should require between 1-2 canisters per year dependent on dose, any requests above this should trigger a review with the patient.
- Administered by the patient herself, onto clean, dry, healthy skin on the sites indicated by the manufacturer. Applied immediately onto the skin. Allow drying for at least 3-5 minutes before dressing. Wash hands with soap and water after applications.

Duration of treatment

- Testosterone therapy should be considered as a trial, which should not be continued if a woman has not experienced a significant benefit by 3 months.
- Usually treatment takes up to 3 months to be effective, so a 3 month follow up is arranged and then 3 monthly follow up appointments continue until a woman is established on treatment.
- 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.

Contraindications

- During pregnancy and breastfeeding
- Hypersensitivity to the active substance(s) or to any of the excipients listed in the product
- Known or suspected carcinoma of the breast and the prostate.

Cautions

- Severe cardiac, hepatic, or renal insufficiency or ischaemic heart disease; as may cause severe complications characterised by oedema with or without congestive cardiac failure, hypertension as testosterone may cause a rise in blood pressure
- Caution in renal and 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/hypercalciuria developing from androgen therapy.
- Epilepsy and migraine
- Thrombophilia; some post-marketing studies and reports of thrombotic events

- Competitive athletes – care must be taken to maintain levels well within the female physiological range
- Women with upper level or high baseline testosterone levels / FAI.
- Risk of testosterone transfer: close skin contact with the area of application by a partner or child should be avoided.
- Randomised studies have not shown an increased risk of cardiovascular disease or breast cancer with testosterone replacement although longer term follow up studies are lacking.

Drug Interactions

- **Anticoagulants**: the anticoagulant effect can increase. Patients receiving warfarin require close monitoring of their INR especially when the androgen treatment is started, stopped or the dose is changed**.**
- Concurrent administration of testosterone with **ACTH or corticosteroids** may increase the likelihood of oedema; thus these drugs should be administered with caution, particularly in patients with cardiac, renal or hepatic disease.
- Androgens may decrease concentrations of thyroxin-binding globulin, resulting in decreased total T4 serum concentrations and increased resin uptake of T3 and T4. Free thyroid hormone concentrations remain unchanged however, and there is no clinical evidence of thyroid dysfunction.

Monitoring requirements

- Monitoring of testosterone therapy specifically should include subjective assessments of sexual response, desire, and satisfaction as well as evaluation for potential adverse effects.
- Monitor FAI/SHBG at baseline, 3 months then every 6 months..
- Monitor for symptoms of excessive androgen exposure such as irritability, nervousness, weight gain.
- BASHH Guidelines state that it is good practice to measure fasting lipid and glucose levels after six months of therapy, if clinically indicated (e.g. by diabetes or hyperlipidaemia).

Adverse effects

- 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)

Information given to patients

See local patient information leaflet (appended)

Cost of treatment

Tostran® pump (testosterone 2% gel) 10 mg per actuation 60g (£28.63) Cost per 28 days: £3.34

Note: Testogel sachets was not recommended for use in women with low libido because of the practicalities for patients needing to measure a 1/10th of a sachet and/or storage of the opened sachet.

Androfeme (1% w/v testosterone cream) is licensed in Australia for management of hypoactive sexual desire dysfunction (HSDD) in postmenopausal women but is not licensed in the UK or available on the NHS.

References

1) Summary of product characteristics (Tostran 2% gel).
2) National Institute of Health and Care Excellence (NICE) Guidelines [NG23]: Menopause: diagnosis and management. Last updated December 2019.
3) NICE Clinical Knowledge Summary: Menopause Last revised November 2020.
4) General Medical Council (GMC): Good practice in prescribing and managing medicines and devices (2013).
5) Medicines and Healthcare products Regulatory Agency (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
6) British Society for Sexual Medicine. Guidelines on the management of sexual problems in women: the role of androgens [Internet]. 2010 [cited 2016 Jan 20]. Available from: https://www.bashhguidelines.org/media/1096/3117.pdf
7) British Menopause Society: Testosterone replacement in menopause – tools for clinicians.
8) Coventry & Warwickshire Area Prescribing Committee Drug Position Statement: Transdermal Testosterone for low libido in Menopausal (both natural and surgical) Females (Oct 19) https://www.covwarkformulary.nhs.uk/docs/chapter06/DPS098-Testosterone%20transdermal%20preparation.pdf?UNLID=92004236520217210959
9) Clayton et al; Mayo Clin Proc 2018 Apr;93(4):467-487 International Society for the Study of Women's Sexual Health Process of Care for Management of Hypoactive Sexual Desire Disorder in Women https://www.mayoclinicproceedings.org/article/S0025-6196(17)30799-1/fulltext

NHS
North Yorkshire & York Area
Prescribing Committee

Testosterone gel (Tostran 2%) for low sex drive in menopausal and post-menopausal women
Information for Patients

Introduction
This leaflet provides information about use of testosterone gel Tostran 2%, for menopausal and post-menopausal women who have a low sex drive (libido). Testosterone is currently not licensed to women in the UK. The use of this gel is 'off label' which means that the manufacturer of the medicine has not applied for a license or has not specified that it can be used in this way. However, it has proven benefits in clinical trials and is also recommended by the National Institute for Health and Care Excellence (NICE).

What is testosterone?
Testosterone is one of the sex hormones produced naturally from ovaries and adrenal glands in women. It is commonly thought of as a male hormone, but testosterone plays an important role in a women's life including desire for sex. Levels of testosterone gradually go down as women get older, but there is a sudden loss of testosterone if you have an operation to remove your ovaries (oophorectomy). When a woman's level of testosterone decreases, she may find that she desires sex less often. There is some evidence that having lower testosterone levels can also affect your mood and increase your risk of being depressed.

What are the potential benefits of testosterone gel?
Testosterone may improve libido, mood, energy, and concentration. Low libido may improve with oestrogen therapy alone, but in some cases testosterone may be more helpful, especially in women who have had their ovaries removed. According to the National Institute for Health and Care Excellence (NICE) guidelines on menopause management, use of testosterone for women who are already taking hormone replacement therapy (HRT) may be helpful. It can sometimes take a few months for the full effects of testosterone to work.

How is testosterone gel used?
Tostran 2% testosterone gel comes in a canister. Pressing the pump once releases a pea sized amount equal to a 10mg dose which needs to be applied initially twice a week but may be increased to every other day by your doctor.
The gel should be rubbed onto dry, non-hairy areas such as the inner surface of forearms or thighs.
The area should be allowed to dry before getting dressed and should not be washed for 2 to 3 hours after applying the gel.
You should keep changing the area where you apply the gel to avoid hair growth in that area.
Hands should be washed immediately after applying the gel to the body.

The area of your skin should not come into contact with partners, children and pregnant women within 1 hour of application.
Do NOT use the amounts stated in the packet's leaflet as this is how much a man should use.

What are the side effects?

Clinical studies have shown that if you follow the instructions carefully, most people can benefit from testosterone gel. Possible side effects are:

- increased facial or body hair (hirsutism) – uncommon
- male pattern hair loss (alopecia) which could be patchy or at the front – uncommon
- acne and greasy skin – uncommon
- deepening of voice – rare
- enlarged clitoris - rare

So far clinical studies have not shown an increased risk of heart disease or breast cancer, but more research is required in this field.

Is blood test monitoring required?

Blood tests are not able to diagnose whether or not you need testosterone but are used as a safety check to ensure you are not getting too much on top of your own natural levels. Blood tests will be carried out before starting, and repeated after 3 months on treatment then 6 monthly. If you find that testosterone is helpful then you would normally continue to use this while you are taking the standard HRT.

When should testosterone gel not be used?

Testosterone should be avoided:

- during pregnancy or breastfeeding
- if you have active liver disease
- if you have a history of hormone sensitive breast cancer
- if you are a competitive athlete
- for women with upper normal limits or high baseline free testosterone levels /Free Androgen Index (>5%)

Further Information

The British Menopause Society: www.thebms.org.uk
Women's Health Concern: www.womens-health-concern.org
Menopause Matters: www.menopausematters.co.uk