BSW use of testosterone as part of HRT in women commissioning statement: Low priority intervention

Policy Statement

BSW clinical advisory group have determined that the treatment of low libido associated with the menopause in women is a low value intervention. Due to the lack of availability of a licensed product and lack of clarity on monitoring requirements and longer-term safety shared care prescribing by primary care is not an option. However, if a specialist consultant within secondary care wishes to prescribe testosterone for such women, they may do so and will need to prescribe it long-term for the full duration of use, with no prescribing moving out to primary care.

Patients will need to be counselled on the risks and provided with materials as appropriate (e.g. Trust Patient Information Leaflet for unlicensed/off-label meds) in order to give informed consent to the intervention.

If a GP receives a request to prescribe testosterone for a woman as part of HRT as a result of a private consultation, they should assess whether its appropriate to refer the patient for an NHS assessment by a HRT specialist (obs/gynae) rather than prescribe it. Alternatively the patient can seek a private prescription from their private specialist. Topical testosterone is not an expensive medication. Relevant CCG private prescribing policies can be found here: https://www.bathandnortheastsomersetccg.nhs.uk/assets/uploads/2019/06/Private-Treatment-Policy-V3.pdf and http://www.wiltshireccg.nhs.uk/wp-content/uploads/2018/05/Private-treatment-Nov-17final.pdf. This policy will be reviewed in one year's time.

Background

There is currently no licensed treatment for women who complain of lack of libido associated with the menopause following the withdrawal of testosterone implants from the market. Standard HRT including Tibolone should always be tried and when this fails to resolve symptoms, testosterone replacement has historically been used as an alternative option.

NICE have published Menopause Guidance and Management - NICE 2015 Altered sexual function[1]

1.4.8 **Consider** testosterone[1] 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 (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.

Criteria for treatment:

- Testosterone replacement in menopausal women is used if hormone replacement therapy (HRT) alone is not effective. Testosterone gel is used in addition to HRT in this setting.

Review criteria: The BMS advise (link above) 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 trialled for a minimum of 3 months and maximally for 6 months 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 the British Menopause Society.

Prescribing information and monitoring: (RED Traffic-light status on BSW formulary)

Products currently available and used off-label for this indication include:

- Testogel® (1% testosterone gel in 5.0g sachets containing 50mg testosterone): Starting dose 1/10th of a sachet/day = 5mg/day i.e. each sachet should last 10 days. Testogel is already on the BSW formulary for male testosterone replacement (amber with shared care).
- Tostran® 2% is a gel in a pump dispenser, and one measured pump (which contains 10 milligrams of testosterone) is usually used three times a week. Tostran is on the BSW formulary for male testosterone replacement (amber with shared care).

Duration of treatment: The BMS advises minimum of 3 months and maximum of 6 months before reviewing efficacy, as it can take 8-12 weeks for effects to become clinically significant. If testosterone replacement is considered to be effective, it is unclear from the BMS guidance how long this should be continued - they advise at least an annual review, which implies that it may be a long-term prescription.

Current Testogel costs (Drug Tariff Dec 19): 30 x 5g sachets=£31.11 (300 days supply); £38.72/yr/pt

Current Tostran costs (Drug Tariff Dec 19): 60g £28.63 (10mg/0.5g application, 120 applications/bottle/ 40 weeks supply)

Monitoring:

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 (HSDD) / Female Sexual Interest and Arousal Disorder (FSIAD), however there can be practical problems with obtaining these. They recommend that the gold standard would be to measure free testosterone, however a calculation can be performed to work out the Free Androgen Index (FAI) using total testosterone and sex hormone binding globulin (SHBG) levels if free testosterone assays are not available. 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.

Further reading:

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

Efficacy & safety: evidence review

NICE NG23 Menopause: diagnosis and management (Nov 2015)[1] full guidance p97:

8.2.5.2.4 Comparison of testosterone verses no treatment/placebo

Frequency of sexual intercourse

One RCT (n=562) found a significant increase in frequency of sexual activities at 24-week follow-up in menopausal women who received testosterone compared with those who did not receive testosterone. The quality of the evidence for this outcome was low.

Moderate quality evidence from 1 RCT (n=519) found a significant increase in the frequency of satisfying sexual activity at 4-week follow-up in menopausal women who received testosterone compared with those who did not receive testosterone.

Both studies reporting results for the outcome of frequency of sexual intercourse included the majority of women with surgical menopause.

p107 conclusion:

In relation to the other short-term outcomes, limited data was found for the outcome of frequency of satisfying sexual intercourse, but testosterone (10 mg/day; gel) was found to significantly increase frequency compared with placebo **although the majority of women included in these trials were surgically menopausal**. The other evidence identified comparing tibolone versus oestrogen plus progestogen did not show a significant difference in the frequency of satisfying sexual activities. Given the limited availability of evidence, the group incorporated their clinical experience to decide that testosterone, although unlicensed for this indication in women, should only be offered as an option of improving low sexual desire for women in menopause when HRT is not effective.

A recent systematic review and meta-analysis[2] of safety and efficacy of testosterone use in women found that Testosterone is effective for postmenopausal women with low sexual desire causing distress, with administration via non-oral routes (eg, transdermal application) preferred because of a neutral lipid profile. The effects of testosterone on individual wellbeing and musculoskeletal and cognitive health, as well as long-term safety, warrant further investigation.

Overall, testosterone treatment was associated with a small but significant increase in weight, such that patients should be advised of this effect if testosterone treatment is being considered (mean difference 0.48, 95% CI 0.16 to 0.79).

Testosterone treatment administered at doses intended to approximate physiological replacement to levels seen in premenopausal women is associated with a greater likelihood of acne and hair growth, but not alopecia, voice deepening, or cliteromegaly, compared with a comparator or placebo.

Therefore, women who initiate testosterone treatment must be warned that these side-effects can occur and counselled against applying more than the prescribed dose.

AUDIT requirements: Acute trusts should collate data on their patients requiring this treatment in terms of efficacy and safety/side-effects so that the policy can be reviewed in light of the data in one year's time.

References:

1.) Menopause Guidance and Management - NICE 2015 Altered sexual function. https://www.nice.org.uk/guidance/ng23/resources/menopause-diagnosis-and-management-pdf-1837330217413

2.) *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.*