SHARED CARE GUIDELINE

Drug: Testosterone

For hypogonadism due to testosterone deficiency in adult men

Introduction	**Indication (licensed):** Testosterone replacement therapy for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests. **Clinical Background:** Endogenous androgens, principally testosterone, secreted by the testes and its major metabolite DHT, are responsible for the development of the external and internal genital organs and for maintaining the secondary sexual characteristics (stimulating hair growth, deepening of the voice, development of the libido); for a general effect on protein anabolism; for development of skeletal muscle and body fat distribution; for a reduction in urinary nitrogen, sodium, potassium, chloride, phosphate and water excretion. **Background to shared care arrangements:** The best interest, agreement and preferences of the patient should be at the centre of any shared care agreement and their wishes followed wherever possible. Patients should be able to decline shared care if, after due consideration of the options, they decide it is not in their best interests. **Please note:** **The provision of shared care prescribing guidelines does not necessarily mean that the GP must agree to and accept clinical and legal responsibility for prescribing; they should only do so if they feel clinically confident in managing that condition.** **Referral to the GP should only take place once the GP has agreed to this in each individual case, and the hospital or specialist will continue to provide prescriptions until a successful transfer of responsibilities has occurred. The GP should confirm the agreement and acceptance of the shared care prescribing arrangement and that supply arrangements have been finalised. The secondary/tertiary provider must supply an adequate amount of the medication to cover the transition period. The patient should then be informed to obtain further prescriptions from the GP.** **This shared care guideline excludes:** 1. Unlicensed indications; 2. Formulations of testosterone other than gel for transdermal application.
Form	Gel for transdermal application
Dose and administration (please refer to BNF / SPCs for full details)	**For Tostran®** (1 g of gel contains 20 mg testosterone) Apply 60 mg once daily, subsequent application adjusted according to response; maximum 80 mg per day. **For Testogel® 50mg/5g** Apply 50 mg once daily; increased in steps of 25 mg, adjusted according to response; maximum 100 mg per day. **For Testogel® 16.2mg/g** (One pump actuation delivers 1.25 g of gel containing 20.25 mg of testosterone)

	Apply 40.5 mg once daily; increased in steps of 20.25 mg, adjusted according to response; maximum 81 mg per day. **For Testavan® 20mg/g** (One pump actuation delivers 1.15 g (1.25 mL) of gel equivalent to 23 mg of testosterone) Apply 23 mg once daily, subsequent dosing adjusted according to response; maximum 69 mg per day. **Individual product summary of product characteristics (SPCs) or patient information leaflets (PILs) should be consulted for detailed application instructions.**
Common Adverse Effects (please refer to BNF / SPCs for full details)	**Common or very common:** Acne; application site reaction; androgenic effects; anxiety; arthralgia; asthenia; changes in libido; cholestatic jaundice; depression; electrolyte disturbances; excessive duration of penile erection; excessive frequency of penile erection; gastro-intestinal bleeding; gynaecomastia; headache; hirsutism; hypercalcaemia; hypertension; increased bone growth; irritability; male-pattern baldness; muscle cramps; nausea; nervousness; oedema; paraesthesia; polycythaemia; precocious sexual development in pre-pubertal males; premature closure of epiphyses in pre-pubertal males; prostate abnormalities; prostate cancer; pruritus; PSA increased; seborrhoea; sodium retention; vomiting; weight gain. Changes in laboratory tests (lipids). Increase in haematocrit, red blood cell count increase, haemoglobin increase. Mastodynia (breast pain). Dizziness. Amnesia. Hyperaesthesia. Mood disorders. Diarrhoea. Alopecia. Urticaria. **Rare:** Liver tumours **Frequency not known:** Dyspnoea. Sleep apnoea. Suppression of spermatogenesis. Electrolyte changes. Jaundice and liver function test abnormalities. Urination impaired, urinary tract obstruction **Please refer to the SPC or BNF for full list.**
Contraindications / Cautions (please refer to BNF / SPCs for full details)	**Contraindications:** Breast cancer in males; history of liver tumours; hypercalcaemia; prostate cancer. Known hypersensitivity to the active substance or any of the excipients listed in the SPC (see individual product SPCs). **Cautions:** Cardiac impairment; diabetes mellitus; elderly; epilepsy; hypertension; ischaemic heart disease; migraine. Pre-pubertal boys (fusion of epiphyses is hastened and may result in short stature)—statural growth and sexual development should be monitored. Skeletal metastases—risk of hypercalcaemia or hypercalciuria (if this occurs, treat appropriately and restart treatment once normal serum calcium concentration restored). Sleep apnoea; stop treatment or reduce dose if severe polycythaemia occurs. Tumours—risk of hypercalcaemia or hypercalciuria (if this occurs, treat appropriately and restart treatment once normal serum calcium concentration restored). Thrombophilia—increased risk of thrombosis. **Potential testosterone transfer:** **If no precaution is taken, testosterone gel can be transferred to other persons by close skin to skin contact, resulting in increased testosterone serum levels**

	and possibly adverse effects (e.g. growth of facial and/or body hair, deepening of the voice, irregularities of the menstrual cycle) in case of repeat contact (inadvertent androgenisation). **The patient should be informed about the risk of testosterone transfer and about safety instructions present in the PIL. Testosterone gel should not be prescribed in patients with a major risk of non-compliance with safety instructions (e.g. severe alcoholism, drug abuse, severe psychiatric disorders).** **This transfer is avoided by wearing clothes covering the application area or showering prior to contact.**
Potentially Serious Drug Interactions (please refer to BNF / SPCs for full details)	**Oral anticoagulants:** Changes in anticoagulant activity (the increased effect of the oral anticoagulant by modification of coagulation factor hepatic synthesis and competitive inhibition of plasma protein binding): Increased monitoring of the prothrombin time, and INR determinations, are recommended. Patients receiving oral anticoagulants require close monitoring especially when androgens are started or stopped. **Corticotrophin (ACTH) and corticosteroids:** Concomitant administration of testosterone and ACTH or corticosteroids may increase the risk of developing oedema. As a result, these medicinal products should be administered cautiously, particularly in patients suffering from cardiac, renal or hepatic disease. **Interaction with laboratory tests:** Androgens may decrease levels of thyroxin binding globulin, resulting in decreased T4 serum concentrations and in increased resin uptake of T3 and T4. Free thyroid hormone levels, however, remain unchanged and there is no clinical evidence of thyroid insufficiency.

Secondary Care Responsibilities	1) Testosterone replacement therapy must be initiated by an endocrinologist in secondary care following confirmation of the diagnosis of hypogonadism after clinical examinations and biochemical tests. 2) Record the person's preferences and concerns in their treatment plan. Patients should be able to decline shared care if, after due consideration of the options, they decide it is not in their best interests. Patients should provide explicit consent and this should be recorded in both the patients notes and on the shared care agreement form. 3) Provide information about the medication to patients, including common side effects, necessary monitoring, and where that monitoring will take place. Also, to keep the patient informed of the process at all stages to ensure continuity of treatment. 4) Titrate the dose against symptoms and adverse effects until dose optimisation is achieved, that is, reduced symptoms etc. 5) Continue all necessary physical health monitoring during the titration period and to monitor effectiveness of medication for and adverse effects, and document in the person's notes. 6) Prescribe and monitor the patient for a minimum period of three months and until the patient is on a stable dose. 7) Continue to provide prescriptions until a successful transfer of responsibilities to the GP has occurred. The secondary/tertiary provider must supply an adequate amount of the medication to cover the transition period. 8) Once Part 2 of the Shared Care Agreement Form has been returned completed and signed by the patients GP, the patient should then be informed to obtain further prescriptions from the GP after the transition period and must be made fully aware of all necessary monitoring requirements. 9) Conduct an annual face to face medication review for all patients covered by this shared care guidance. 10) Contact the GP within 3 days of a patient missing a specialist face to face appointment to advise whether treatment should be withheld 11) Accept referrals back from primary care for medication discontinuation. 12) Resume prescribing and monitoring of the patient when a decision for managed withdrawal of treatment has been taken. 13) Continue to provide emergency appointments where patients are receiving prescriptions from their GP and they feel that a prompt assessment or review of their treatment is required. 14) Provide prompt on-going advice to General Practitioners as required without necessarily requiring a new referral. 15) Provide advice to the GP as to the changes in parameters that should trigger urgent referral back to the specialist 16) Telephone details and (if appropriate) secure email addresses for both Secondary and Primary Care should be exchanged and recorded. This should include out-of-hours contact numbers. Patients and their carers should also be provided with contact details for support and help if required; both in and out of hours. 17) Ensure that adequate training and educational support is in place for the primary care multidisciplinary team (in collaboration with the local commissioner of the service pathway i.e. CCG)
Primary Care Responsibilities	**Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.** 1) To consider requests to prescribe under shared care arrangements and reply in a timely manner by completing, signing and returning Part 2 of the Shared Care Agreement Form.

2) To provide continuation prescriptions or identify any concerns about the request to the prescriber in the specialist team. It is expected that primary care prescribers will not make changes to the dose/formulation, unless it is in consultation with the specialist team.

3) To monitor the patient as outlined below and contact the specialist team if results give rise to concern. Any ongoing monitoring requirements for individual patients discharged from secondary care will be identified by the specialist service as part of the discharge information to the GP.

4) To contact specialists within the team where concerns arise about a patient's presentation or when advice is needed.

5) To refer to secondary care if withdrawal of treatment might be indicated.

Circumstances for discontinuation of treatment in Primary Care

1) As a joint decision with specialist team providing specific advice in case of adverse effect pending assessment.

2) Following non-attendance at annual specialist team review pending that review taking place or if there is failure to engage with the review process.

Monitoring

Secondary care should prescribe and monitor the patient for a minimum period of three months and until the patient is on a stable dose.

Monitoring Required	Schedule
Haematocrit*	Monitored at six weeks, then again at three months then as directed by the specialist service.
Serum Oestradiol*	Monitored at six weeks, then again at three months then as directed by the specialist service.
Haemoglobin**	Before treatment, every three months for the first year, and yearly thereafter.
LFTs**	Before treatment, every three months for the first year, and yearly thereafter.
Lipids**	Before treatment, every three months for the first year, and yearly thereafter.
Prostate and PsA**	Before treatment and once yearly thereafter (twice yearly in the elderly).
Testosterone*	Baseline and at regular intervals as directed by the specialist service. However, it is expected that testosterone levels would be monitored at six weeks, then three, six and 12 months after starting therapy and annually thereafter. **Please note:** assess T concentrations 2–8 h following the gel application. Clinicians should maintain serum testosterone concentrations during treatment in the mid-normal range for healthy young men (local reference ranges should be used).

* Recommended by the specialist endocrinology service, UHMB

** Recommended by the SPC

Bibliography

1. Summary of Product Characteristics. Testosterone gel 50mg in 5gram (Testogel). Besins Healthcare. Updated: 12/12/17. Accessed via: https://www.medicines.org.uk/emc/product/6808/smpc [Accessed online: August 2018].
2. Summary of Product Characteristics. Testosterone transdermal gel 20 mg/g (Testavan). Ferring Pharmaceuticals Limited. Updated: 15/02/18: Accessed via: https://www.medicines.org.uk/emc/product/9489 [Accessed online: May 2019].
3. Summary of Product Characteristics. Testosterone gel 20.25mg in 1.25gram (Testogel). Besins Healthcare. Updated: 30/07/18. Accessed via: https://www.medicines.org.uk/emc/product/8919/smpc [Accessed online: August 2018].
4. Summary of Product Characteristics. Testosterone gel 10mg in 0.5gram (Tostran 2% gel). Kyowa Kirin Ltd. Updated: 20/02/17. Accessed via: https://www.medicines.org.uk/emc/product/332/smpc [Accessed online: August 2018].
5. Royal Pharmaceutical Society. British National Formulary. Online. Accessed via: www.evidence.nhs.uk. [Accessed online: August 2018].
6. Bhasin et al. Testosterone Therapy in Men With Hypogonadism: An Endocrine Society Clinical Practice Guideline. Journal of Clinical Endocrinology and Metabolism. May 2018, 103(5):1715–1744.

Version Number	Date	Amendments Made	Author
Version 1.1	July 2019	Added Testavan®. Deleted Testim®.	DP

Midlands and Lancashire Commissioning Support Unit,
Jubilee House, Lancashire Business Park, Leyland, PR26 6TR
Tel: 01772 214 400 | www.midlandsandlancashirecsu.nhs.uk