SHARED CARE AGREEMENT

Name of medicine	*Masculinising Endocrine Treatment (Testosterone)*
Indication	*Gender dysphoria/incongruence after assessment at the GIC for over 18 year olds*

Version: 1.0 Approval date: **September 2024** Review date: **September 2027**

The Shared Care Agreement (SCA) is intended to facilitate the accessibility and safe prescribing of complex treatments across the secondary/primary care interface. It does not contain all of the relevant product information, which should be sought using the current British National Formulary and manufacturer's Summary of Product Characteristics. The SCA must be used in conjunction with the NHS Lothian Procedure for the Shared Care of Medicines, available here.

Roles and responsibilities

Chalmers Gender Identity Clinic (GIC) will undertake initial assessment and recommending establishment of treatment for all those seeking masculinising endocrine treatment. GPs will be asked to be undertake the prescribing and reporting of any issues to the GIC.

However, recall and monitoring will be undertaken by the GIC, who will also undertake any clinical review required. The GP will then be asked to prescribe accordingly. This has now been agreed with the Lothian GP Sub-Committee. It has also been agreed that GPs will undertake a pre-dose testosterone level for those on depot preparations (please see below for further detail) as a trough measurement is needed.

This document uses the term **trans men** to include trans men and non-binary people recorded female at birth using masculinising hormones in connection with gender dysphoria or incongruence. This guidance is for adults aged 18 and over.

Listed below are specific responsibilities that are additional to those included in the NHS Lothian Policy and Procedures for Shared Care. Please refer to the policy for core roles and responsibilities that apply to all Shared Care Agreements.

Consultant

INITIAL SPECIALIST ASSESSMENT - GIC:

- Baseline assessment, treatment counselling, gaining informed consent, and recommendation of initiation of treatment (communicated to GP to be prescribed). This will include consent for the unlicensed use of medications
- Provide information both to the GP and the patient outlining risks of treatment
- Patient - signed agreement with the specialist about use of unlicensed medications, copied to the GP
- Assess the need for contraception, and prescribe/refer accordingly (reproductive age)
- Monitoring (usually 3 monthly) for the first year (or until patient on a stable medication regimen)
- Communication with GP about any changes in treatment
- Referral for specialist interventions relating to gender reassignment and transitioning
- Referral for non-specialist interventions as suggested by the GIC (e.g. CMHT, weight management etc)
- Advise about changes in CHI
- Discussion of relevant screening programmes details available from national screening programmes (cervical for those with an intact uterus; breast – may not be required if mastectomy has been performed)
- Cardiovascular risk assessment: ASSIGN
- There should be no need for additional bone protection, except in the rare situation of someone having had gonadal removal who is not also taking hormonal therapy. Please note the advice about Vitamin D in Scotland and on standard osteoporosis management.

ONGOING CARE (SHARED)

The following will be organised by the GIC who will recall all patients annually:

- 12 monthly monitoring: FBC (Hb & haematocrit) for all on testosterone treatment
- Testosterone levels for those on transdermal treatment (2-4 hours after dosing)
- From age of 50, 5 yearly BP measurement and full lipid profile for ASSIGN
- For those on injectable testosterone a trough sample is required immediately prior to injection, and it has been agreed with the GP Sub-Committee that this will be done by the GP team giving the injection. In due course it is proposed there will be an electronic method of ensuring that this result goes to the GIC. In the interim the GIC will advise arrangements

which may be the use of a paper form with destination Chalmers Gender Identity Clinic for the result. The bloods required are testosterone and FBC.

GIC ANNUAL REVIEW:

The patient will be offered a review. This may be virtual with the option of Patient-Initiated Follow up (PIFU) with GIC if there are interim clinical issues, thereby retaining specialist clinical oversight:

- Review of response to treatment, as indicated;
- Review of all the blood results as above, and 5 yearly ASSIGN score in those aged over 50;
- Discuss and encourage healthy lifestyle in line with standard advice – smoking cessation, maintaining a healthy weight, drinking alcohol according to national guidance (maximum 14 units per week), exercising regularly and eating well. Further advice is available at: https://www.nhs.uk/live-well/
- Communicate any incidental findings
  Incidental blood abnormalities detected on baseline screening or follow up that are not related to gender issues or unrelated to proposed or current hormone treatment (ie neutropenia/neutrophilia): GIC will ask GP to repeat and manage as per local guidance
- Communicate outcome to patient and GP, including any changes in medication, or non-attendance for required checks when prescribing would be reviewed.

General Practitioners and primary care non-medical prescribers

GENERAL PRACTITIONER RESPONSIBILITIES:

Prescribing of gender affirming hormones as advised by the GIC and reporting of any issues to the GIC

- Undertake annual trough testosterone bloods and FBC for those on injectable testosterone medication (see above)
- Cervical screening as for standard guidelines (requires sensitive discussion taking into account the patient's dysphoria)
- Assess the need for contraception, and prescribe/refer accordingly (reproductive age)
- Prescribing of treatment as per GIC advice
- Inform the GIC if there is a new diagnosis of liver, breast or other hormone-dependent cancer
- Inform the GIC if there is a diagnosis of severe liver, renal or cardiac insufficiency, or new onset IHD (or other new cardiovascular diagnosis), diabetes or rheumatoid arthritis

Opportunistically encourage healthy lifestyle in line with standard advice – smoking cessation, maintaining a healthy weight, drinking alcohol according to national guidance (maximum 14 units per week), exercising regularly and eating well.

Patient, relatives, carers

To attend for monitoring as requested.

To keep the GIC updated of any change to their name, address or phone number.

Support and Advice for the GP and primary care non-medical prescribers

Support and Advice for the GP

The GIC can be contacted by health professionals only for advice via SCI Gateway for Chalmers Sexual Health Centre, Gender Identity, otherwise clinical advice is available by email at loth.gic@nhs.scot. Referrals are viewed weekly and we will answer any queries within 7 working days. For more urgent advice you can phone the service admin team on 0131 5361570.

Hormone therapies are recommended under the Endocrine and Fertility Preservation Guidance 2022, based on the Scottish Government Gender Reassignment Protocol 2012. This advice is regularly updated by the clinical network (NCGICNS) and the latest is available at Endocrine Guidance – National Gender Identity Clinical Network for Scotland

Hormonal therapy may be recommended after the initial assessment is completed and the Lothian approach to prescribing and monitoring is supported by a multidisciplinary expert team.

New Patients

Some people will have been assessed by, or had treatment from, a recognised NHS gender identity clinic and are new to Borders, Fife or Lothian (the areas served by the GIC). If they have been assessed by an NHS GIC (or specialist gender service whilst resident overseas) the GIC can provide email advice on ongoing treatment or see patients where that is necessary. The GIC is unable to prioritise patients who have accessed private treatment and recommends that they are advised to continue their engagement with their existing provider until the GIC has completed its assessment.
For those moving into Scotland, please advise about the procedures for changing CHI numbers
and enrolling in the relevant national screening programmes. CHI numbers are gender specific, the penultimate number of the CHI signifying female (even number) or male (odd number).

Key Information on the Medicine

Refer to current edition of the British National Formulary (BNF), available at www.bnf.org, and Summary of Product Characteristics (SPC), available at www.medicines.org.uk for detailed product and prescribing information and specific guidance.

BACKGROUND - TESTOSTERONE

The literature for use of masculinising hormones is limited, but continues to evolve, and this guidance will be amended as new evidence emerges. The research is hampered by confounding factors, and that historically a variety of hormone doses and preparations have been used. Many of the recommendations for monitoring come from American practice, often over-cautious in relation to the available evidence. There is some internationally recognised guidance for monitoring, but it too has limitations and the recommendations in this document reflect a pragmatic multi-disciplinary consensus view.

There is now a growing - and reassuring - evidence base around the safety of testosterone used for gender reassignment. This now demonstrates that generally the risks are those of (physiological) replacement therapy in men with hypogonadism, as are the monitoring requirements. There are no prospective trials assessing risk, but retrospective cohort studies indicate a probable small rise in some cardiovascular markers (such as non-calcified plaque) but not in cardiovascular events. The largest of these was well-validated, but involved a young population[i], so we suggest vigilance remains necessary in older groups and those with other cardiovascular risk factors until prospective evidence becomes clearer. However, any additional risks are small, particularly when compared with the baseline prevalence. We therefore recommend standard healthy lifestyle approaches, and ASSIGN scores in older age groups to optimise blood pressure and lipid management in lines with standard care. But this is not a clinical indication to limit or stop testosterone use. There is no evidence of raised VTE risk.

There are limited data on the long-term health risks of hormone treatment and patients should be made aware that this is the case and the importance of long-term monitoring. However, evidence strongly supports the use of interventions in gender dysphoria for better clinical outcomes when the emotional and psychological risk versus benefit to the patient is accounted for. Risks may change over the course of a lifetime and need to be reassessed where new morbidities become apparent. The majority of people currently using masculinising treatment are young.

This is an unlicensed use of testosterone (except for Sustanon®), so the Summary of Product Characteristics relates to use in non transgender men, in whom breast cancer, and current or previous liver tumours are listed as contraindications.

Most trans men will not require GnRH analogues with masculinising hormones. If this does happen, please refer to the feminising treatment guidance for further detail.

In particular there is NO indication for the following checks or screening:

- Cardiovascular risk assessment in those aged under 50
- Routine liver function testing
- Osteoporosis screening
- Pituitary tumours (there seems to be a small rise in somatotrophinomas, but these are excessively rare)
- Change of dose in older age.

There needs to be caution about prescribing with cardiovascular co-morbidity, but there will be an initial assessment of this made at therapy initiation. However, it is thought that overall, the additional risks brought by testosterone are very low in healthy individuals and that there only needs to be a further assessment made if the person acquires a significant new cardiovascular diagnosis or risk factor such as diabetes or rheumatoid arthritis. Currently, most people receiving testosterone therapy for gender transition are low risk because they are young.

Please note that the GIC can also provide email advice, available to professionals only.

Please note that NEITHER TESTOSTERONE NOR GnRH analogue treatments PROVIDE CONTRACEPTION.

Testosterone is teratogenic and so effective contraception is recommended where appropriate to prevent unintended pregnancy unless bilateral oophorectomy or hysterectomy has been undertaken. Neither testosterone therapy nor gonadotrophin releasing hormone (GnRH) analogues are contraceptive.

Suitable contraception:

- All progestogen only methods (Implant, injectable, progesterone-only pill)
- LNG IUD
- Copper IUD

All methods of emergency contraception (CU-IUD, ulipristal, levonorgestrel) can also be used.

NB Combined hormonal methods should not be used as estrogen counteracts masculinising effects of testosterone.

The Faculty of Sexual and Reproductive Healthcare (RCOG) provides guidance on contraceptive choices for transgender and non-binary people.

Exogenous testosterone:

- The most common side effect is polycythaemia with raised haematocrit (risk is related to peak testosterone levels, so more common with short-acting injectable preparations, less common with transdermal administration)
- Administration of any oily depot preparation can very rarely cause Pulmonary Oil Microembolism – POME. This can be avoided by injecting very slowly over two minutes
- The manufacturers advice is that it is contraindicated in those with severe cardiac, renal or hepatic insufficiency, or IHD
- May increase coumarin anticoagulant activity – *increased INR monitoring is recommended at times of dose changes.*

Indication

Treatment of gender dysphoria following assessment at the GIC.

Dosage and administration

Introduction & titration: - undertaken by the GIC, with advice to GPs about prescribing

- Tostran® 2%, 10 or 20mg (1 or 2 'presses')/day may be titrated up to 80mg (8 'presses')/day
  OR
- Testogel® 16.2mg/g, 20.25mg/day (1 press) may be titrated up to 60.75mg/day (3 presses)
  OR
- Testogel® 40.5mg/2.5g, ½ or 1 sachet, may be titrated up to 2 sachets/day
  OR
- Testogel® 50mg/5g, ½ or 1 sachet, may be titrated up to 2 sachets/day
  OR
- Testavan® 2% gel 23mg (1 press) may be titrated up to 69 mg/day (3 presses)
  OR
- Sustanon® by injection, 125mg every 2-4 weeks for 2-3 months, increase to 250mg every 2-4 weeks if tolerated and testosterone levels sub-therapeutic. This should be injected slowly over 2 minutes.

Testosterone undecanoate injections have a longer half-life than other preparations so can help stabilise the small number of people who are chaotic with their treatment.

After 6 months, or once stable, patients either continue on the treatment they are on or offered the following maintenance treatments.

Maintenance:

- Testosterone undecanoate 1000mg deep intramuscular injection over at least 2 minutes usually every 10-14 weeks according to GIC recommendations **OR**
- Transdermal testosterone according to GIC recommendations **OR**
- Sustanon® intramuscular injection 125-250mg (NOT in the deltoid) every 2-3 weeks according to GIC recommendations.

Oral testosterone preparations are **not** recommended.

Decisions to adjust doses should be undertaken by the GIC.

Monitoring **Introduction & titration:** - undertaken by the GIC, with advice to GPs about prescribing

- Tostran® 2%, 10 or 20mg (1 or 2 'presses')/day may be titrated up to 80mg (8 'presses')/day
  OR
- Testogel® 16.2mg/g, 20.25mg/day (1 press) may be titrated up to 60.75mg/day (3 presses)
  OR
- Testogel® 40.5mg/2.5g, ½ or 1 sachet, may be titrated up to 2 sachets/day
  OR
- Testogel® 50mg/5g, ½ or 1 sachet, may be titrated up to 2 sachets/day
  OR

- Testavan® 2% gel 23mg (1 press) may be titrated up to 69 mg/day (3 presses).
  OR
- Sustanon® by injection, 125mg every 2-4 weeks for 2-3 months, increase to 250mg every 2-4 weeks if tolerated and testosterone levels sub-therapeutic. This should be injected slowly over 2 minutes.

Testosterone undecanoate injections have a longer half-life than other preparations so can help stabilise the small number of people who are chaotic with their treatment.

After 6 months, or once stable, patients either continue on the treatment they are on or offered the following maintenance treatments.

Test Testosterone ***(if transdermal treatment)***	Annually	Normal: 8.6-29nmol/L	The GIC will action: standard advice is to recheck to for persistent elevation.
Testosterone trough levels ***(if parenteral treatment)*** ***GP Practice to undertake prior to injection***	Annually	Abnormal: < 9nmol/L or >15nmol/L	The GIC will action: standard advice is to defer next injection by 2 weeks; if persistently above 20nmol/L, dose review is required.
FBC (Hb and haematocrit) ***GP Practice to undertake prior to injection (alongside testosterone level)***	Annually	Abnormal: Haematocrit > 0.52	The GIC will action. The following is standard advice: there are often minor rises in haematocrit which can be ignored. Increasing injection interval or changing to transdermal preparation can be effective. Consider referral to haematology for assessment and rarely venesection. *PLEASE ENSURE THE MALE REFERENCE RANGE IS BEING USED –see gender-specific reference ranges for blood tests.*
INR	Increased monitoring at time of dose change if coumarin anticoagulants used		Adjust warfarin dose accordingly.
Cardiovascular health	Age <50, maximise opportunities to give healthy lifestyle advice. Age >50, 5 yearly ASSIGN score.		The GIC will advise treating blood pressure and adverse lipid profiles in line with standard national guidance. GPs are reminded to seek GIC advice if new onset cardiovascular disease, diabetes or other concern about significant new risk.
Screening	Consider that breast and cervical screening may still be needed.		For specific transgender advice, please see: national screening programmes

Cautions, contraindications - Refer to current Summary of Product Characteristics: www.medicines.org.uk

Fertility, Pregnancy and Lactation

Refer to current Summary of Product Characteristics: www.medicines.org.uk for full detail.

Vaccination

Adverse effects - Refer to current Summary of Product Characteristics: www.medicines.org.uk for full detail.

Drug interactions - Refer to current Summary of Product Characteristics: www.medicines.org.uk for full detail.

The presence of this SCA does not compel a primary care prescriber to prescribe if they feel that it is out with the scope of their competencies (as per GMC guidance on safe prescribing) or resources, as ultimate responsibility lies with the prescribing, not the recommending, clinician.

For office use only:

Approved by the General Practice Prescribing Committee (GPPC) on 10th September 2024. Minor changes (email address update and broken hyperlink corrected) approved January 2025.

[1] Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons A Cohort Study. Getahun, D. et al. Ann Intern Med. 2018;169:205-213. doi:10.7326/M17-2785.