The Tavistock and Portman
NHS Foundation Trust

SHARED CARE PRESCRIBING GUIDANCE

Treatment of Gender Incongruence in Transgender men, Transmasculine and Non-binary People (Assigned Female at Birth)

Applicable to:	GPs referring clients to the adult Gender Identity Clinic, Tavistock and Portman NHS Foundation Trust
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Principal Author(s):	[redacted] Consultant Endocrinologist [redacted] Clinical Director [redacted] Endocrinologist [redacted] Endocrine Clinical Nurse Specialist
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INTRODUCTION

This document has been prepared by [redacted] Consultant Endocrinologist, and the GIC's Clinical Team.

The information contained in this document has been compiled in order to support GPs and other medical practitioners in safe prescribing and monitoring arrangements. The document outlines the roles and responsibilities of the Gender Specialists, General Practitioners and Clients and contains both a **shared care agreement** and a client **letter of consent** for the initiation of hormones. It is imperative that clients who take the preparations, as listed, do so under medical supervision, and are monitored as recommended.

Please ensure that the latest updates on the medications and interactions, as listed, are obtained from the BNF.

Enduring validity of the principle of shared care:

If we have assessed a patient and on the basis of gender incongruence suggested hormone therapy, the principle of shared care remains valid for the duration of their time under active treatment with our service, and also after discharge. A new shared care document is not required each time we update the guidance, as the principle of shared care remains valid. Inevitably over time on hormone therapy, as with most

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medications, adjustments need to be made in relation to blood test results and clinical response to treatment and we give advice on this in clinic letters and correspondence. We do not send a new shared care document each time a change to hormone therapy dosing or formulation is suggested, because the advice we provide is consistent with the shared care guidelines.

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LETTER FROM CLINICAL DIRECTOR and CONSULTANT ENDOCRINOLOGIST

Dear Colleague

We have created this shared care protocol in order to ensure that clients who attend the Charing Cross Gender Identity Clinic receive a partnership of care from both their Gender Clinicians and their General Practitioners.

The medicine recommended by the GIC is usually a testosterone (e.g. Sustanon) to cause masculinisation, and which will be continued indefinitely after surgery. In some cases additional or alternative medicines are used, as outlined in the shared care protocol. Sometimes there is a need for a GnRH analogue (e.g. Decapeptyl or Zoladex) or progestins to suppress ovarian function prior to surgery.

In view of the fact that clients will be having long-term maintenance treatment, it is in their best interests for their GP to prescribe and monitor their treatment, with support from our clinic as necessary.

Although not all these medicines are licensed for the treatment of gender dysphoria (nor are they likely to be), they are medicines with which, in our experience, GPs will be familiar. The doses of testosterone are the same that would usually be prescribed for hormone replacement in a born male. The one exception to this is Sustanon which is licensed for this indication.

This devolvement of prescriptions to Primary Care is consistent with the GMC guidance on the provision of prescriptions for patients with gender dysphoria in Primary Care. The link for that is as follows:
https://www.gmc-uk.org/ethical-guidance/ethical-hub/trans-healthcare---advice-based-on-gmc-guidance

There is a comprehensive programme for assessment and evaluation of clients referred to this clinic, into which GPs and any relevant secondary care clinicians are routinely copied. When all these assessments have been undertaken, the decision may be taken to recommend medication.

In the event that a written recommendation for hormone therapy is made, we would be grateful if arrangements can be made by the client's GP to see the client within two weeks in order to initiate the treatment.

We hope that this will give GPs enough information to feel confident to prescribe the medication for clients as specified. If you have any questions, or would like more information, you are welcome to contact us.

Yours sincerely,

[redacted]

Clinical Director, Gender Identity Clinic

[redacted]

Consultant and Professor in Endocrinology

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Treatment of Gender Dysphoria in Trans Masculine People

CLINICAL INFORMATION

Indication(s):	Treatment of gender incongruence following psychiatric/psychological assessment at Gender Identity Clinic. <u>Binary gender identities (transgender men):</u> The standard protocol is outlined in this shared care document. <u>Non-binary gender identities:</u> Though based on knowledge and experience of cross-sex hormonal therapies in transgender men and transgender women, our approach to hormone therapy for non-binary clients is multidisciplinary and individualised. An individualised assessment and treatment approach is consistent with WPATH (2022) SOC 8 guidance (1). For clients with a non-binary gender identity, the aims of therapy may be different to the standard aims outlined in this document and as such an individualised care plan will be documented and may be updated over time.
Place in Therapy:	Hormonal therapy will usually be recommended after the initial assessments are complete. Commencement of hormonal therapy is recommended when a secure diagnosis of gender incongruence is made and the person is psychologically and socially stable. The person will be assessed as being capacitous to understand the pros and cons of treatment. Any psychological or physical health complications will be assessed and advice given on optimisation of the individual's psychological and physical health prior to starting on hormone treatment. Clinical practice in the GIC follows a modified version of the WPATH version 8 Standards of Care. The use of hormonal manipulation in the treatment of transgender individuals is hampered by a lack of any randomised controlled trials to assist in our therapeutic decisions. There has, however, been a significant amount of experience in the treatment of this condition over the last 60 years, using several well-established hormonal protocols, and the totality of the available evidence demonstrates that, for carefully selected clients, hormone therapy is a safe and effective means of alleviating the potentially debilitating condition of gender dysphoria (2-5). Indeed, Sustanon is licensed as supportive therapy for transgender men.
Dose & route of administration:	Baseline tests should be done, see below, prior to commencing hormone treatments. **<u>Testosterone to cause masculinisation:</u>** ***First line:***

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Testosterone gels are usually recommended as first line for patients who:

- Have a BMI of 40 kg/m2 or higher
- Smoke/use tobacco (if smoking, use cisgender HRT dosing)
- Have a history of cardiovascular event or risk factors for cardiovascular disease
- Have significant mood instability or impulsivity (as testosterone gel tends to provide more stable testosterone levels day-to-day as compared to injectable formulations).

Short-acting Injectable Testosterone (Sustanon or Testosterone Enantate):

Starting dose: Sustanon 250 mg intramuscular (IM) every 4 weeks. Testosterone Enantate can be seen as equivalent.

Sustanon contains arachis oil so should not be used in clients with nut allergy. Testosterone enantate should not be used in clients with sesame allergy.

The aim of therapy is to achieve trough testosterone levels at the bottom of the normal male range (8-12 nmol/l) on the day of the injection, just before it is administered, and to achieve peak testosterone levels in the high normal male range but less than 30 nmol/l one week after the injection.

After initiating therapy, **the first set of monitoring bloods** should be performed at the time of the 4th injection (in the steady state), as trough and peak blood tests, as per the following instructions:

- **Trough** blood test (taken on the day of injection **BEFORE** the injection is administered): testosterone (aim 8-12 nmol/L), full blood count, fasting lipids, liver function tests

- **Peak** blood test (taken one week **AFTER** injection): testosterone only (aim <30 nmol/L)

- **Blood pressure** and **BMI**

Dose titration and repeat monitoring blood tests:

Doses of these short-acting testosterone preparations at 250 mg 2-4 weekly are usually adequate to suppress menstruation when therapy is optimised (i.e., when trough and peak testosterone values are in range (as above)). Maximum injection frequency is every 7 days.

Titration of the trough value is achieved by adjusting the length of time between the injections, usually by weekly intervals [6]. Titration of the peak value is achieved by adjusting the dose administered with each injection, by 50 mg increments (0.2 ml of 1ml vial) each time.

Focus on the trough level first. If both trough and peak levels are too high it is best to adjust the injection frequency first and then the dose.

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Monitoring should be performed in the steady state, at the time of the 4th injection (after initiating treatment, or after any change to the dose or frequency). Both the trough and peak testosterone levels need to be measured as above.

Additionally, m*onitoring should be done every 3-6 months in the first year, every 6-12 months in the second year, and then annually thereafter if therapy is stable*.
The GIC can advise on dose titration and adjustments to therapy, on receipt of blood test results and other monitoring information.

Topical testosterone gel preparations, dose range 20-100 mg once a day:

Testogel 16.2 mg/g gel (one actuation of pump = 20.25 mg testosterone)
Tostran 2% gel (one actuation of pump = 10 mg testosterone)
Testavan 20 mg/g gel (one actuation of pump = 23 mg testosterone)

The usual starting dose is approximately 40 mg daily:
2 pump actuations of Testogel 16.2 mg/g once a day (40.5 mg testosterone)
4 pump actuations of Tostran 2% once a day (= 40 mg testosterone)
2 pump actuations of Testavan 20 mg/g once a day (= 46 mg testosterone)

Gel should be applied to the body or legs, avoiding the arms (to prevent contamination of blood samples when blood tests are required).

Hands should be washed after gel application, and the gel should be allowed to dry fully before dressing. Showering/bathing should be avoided for two hours after the gel is applied.

With gels, care must be taken to avoid transfer (by prolonged skin to skin contact) to other people (especially women and children) and to animals for 6 hours after gel application. This will be prevented if the gel is allowed to dry and the area is covered with clothing.

The aim of therapy is to achieve a plasma testosterone in the middle adult range (15-20 nmol/L), 4-6 hours after the gel is applied to the skin. The testosterone level should be measured 4-6 hours after the gel application and there should be no gel applied to the arm on that day[6].

The first set of monitoring bloods is due 8 weeks after initiating therapy, as follows:

- Blood should be drawn for: **testosterone (aim 15-20 nmol/L), full blood count, fasting lipids, liver function tests**.
- The blood test should be taken **4-6 hours after the gel is applied to the skin**, making sure no gel whatsoever reaches the skin from which blood is taken (i.e., mid-arm elbow area).
- **Blood pressure** and **BMI**

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Dose titration and repeat monitoring blood tests:

Dose titration of testosterone gels is achieved by adjusting the number of actuations of the gel pumps, usually by one actuation at a time to achieve a plasma testosterone in the middle adult male range 15-20 nmol/l.

After any adjustment to dose or formulation of testosterone gel, repeat monitoring is due 8 weeks later, as per the above instructions.

Additionally, monitoring should be done every 3-6 months in the first year, every 6-12 months in the second year, and then annually thereafter if therapy is stable.

The GIC can advise on dose titration and adjustments to therapy, on receipt of blood test results and other monitoring information.

Second Line:

Long acting injectable testosterone (Nebido):
In cases where the short-acting injections cause side effects (e.g. mood swings or injection site reactions), and gel preparations are not suitable (i.e. do not give reliable levels, the client is very hirsute, or there is a significant risk of transfer of the testosterone gel to others), the long acting Testosterone Undecanoate (Nebido) may be used[6].

Nebido may be considered as a more cost-effective therapy when the client has been established on testosterone treatment, as it requires fewer GP visits and therefore less clinical time to administer. Nebido as a long-acting preparation requires loading as below:

Please note that Nebido must be administered slowly (over two minutes, as a deep IM injection into the buttock) by a trained healthcare professional in a healthcare environment where there is access to oxygen, due to the very low risk of oil microembolism. See manufacturer's instructions for further information.

The aim of therapy is to achieve a plasma testosterone (measured as a trough sample prior to a Nebido injection) in the lower part of the adult male testosterone range (typically 10-15 nmo/l).

Nebido Loading:
The usual dose is Nebido 1000 mg/4 ml IM. In patients under 55 kg in weight, we usually suggest adjusting the dose to 750 mg/3ml IM.

Stage One:

Nebido 1000 mg/4 mls IM is administered, accompanied by either: Sustanon IM at the current dose (or testosterone enantate), or two weeks of topical testosterone gel at the current dose (Testogel, Tostran, Testavan).

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Thereafter, the Sustanon (or testosterone enantate) or testosterone gel should be stopped.

Stage Two:

Six weeks later Nebido 1000mg/4mls IM is administered.

Stage Three:

Six weeks later Nebido 1000mg/4mls IM is administered.

This completes the loading phase.

Stage Four:
Twelve weeks later, the next Nebido injection AND the **first set of monitoring bloods are due**. After the bloods have been taken, Nebido 1000mg/4ml IM is administered. The bloods should be taken as a trough level, on the day of the injection, prior to the injection, as follows:

- Blood should be drawn for: **testosterone** (aiming 10-15 nmol/L), full blood count, **fasting lipid profile, liver function tests.**
- **Blood pressure** and **BMI**

When all results are available, please send them to the GIC for review and advice on adjustments to therapy.

Stage Five:
Thereafter, Nebido 1000mg/4ml IM is administered every 12 weeks, unless advised otherwise by the GIC.

Dose titration and repeat monitoring blood tests:
The aim of Nebido therapy is to achieve a plasma testosterone (measured as a trough sample prior to a Nebido injection) in the lower part of the adult male testosterone range (typically 10-15 nmo/l). This is achieved by adjusting the injection frequency, usually by a week up or down. The dose is not usually adjusted.

After any adjustment to injection frequency, repeat monitoring is due just before the 3rd injection after the change in therapy (i.e., at the end of the 2nd injection cycle), as per the above instructions.

Additionally, monitoring should be done every 3-6 months in the first year, every 6-12 months in the second year, and then annually thereafter if therapy is stable.

The GIC can advise on dose titration and adjustments to therapy, on receipt of blood test results and other monitoring information.

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Menstrual Suppression

If testosterone therapy to adult male levels does not suppress menstruation or amenorrhoeic cycling, then progestins or GnRH analogues can be used to suppress ovarian function.

Progestins:

Medroxyprogesterone acetate 10 mg B.D or T.D.S [7]

Gonadotrophin Analogues (GnRH analogues):

Decapeptyl (triptorelin) SR 11.25 mg (IM) every 12 weeks (most cost-effective option)

or

Zoladex (goserelin) 10.8 mg (sub cut) every 12 weeks

Alternatives:
Leuprorelin (Prostap) 11.25 mg (IM) every 3 months
Leuprorelin (Prostap) 3.75 mg (IM) monthly
Goserelin 3.75 mg (sub cut) monthly
Decapeptyl SR 3 mg (IM) monthly
Decapeptyl SR 22.5 mg (IM) every 6 months
Nafarelin (Synarel) nasal spray, 200-400 micrograms twice a day (see BNF)

The usual side effect profile of GnRH analogues such as accelerated cardiovascular disease and reduced bone mineralisation and menopausal symptoms do not occur in patients on testosterone treatment at the same time. GnRH analogues may prolong the QT interval and if the patient is taking medications that can prolong the QT interval such as antipsychotic medication they should have an ECG performed before commencing a GnRH analogue.

Treatment of non-binary individuals

For clients with a non-binary gender identity, the aims of therapy may be different to the standard aims outlined in this document and as such an individualised care plan will be documented and may be updated over time. After assessment (including general risks and benefits of hormone treatment) by gender specialists in the core side of the clinic, non-binary clients who opt for hormone therapy are routinely offered appointments in the endocrine department for an individualised discussion of their goals for hormone therapy, taking account of their desired degree of feminisation/masculinisation/androgyny. Based on knowledge and experience of cross-sex hormonal therapies in transgender men and transgender women undergoing a binary transition, our approach to hormone therapy for non-binary clients is multidisciplinary and individualised. An individualised assessment and treatment approach is consistent with WPATH (2022) guidance [1]. To manage expectations and explain limitations of hormone therapy, they are also counselled on what is likely or possible with regard to the usual expected timeframes and outcomes of hormone therapy and possible variations to this, as well as the more permanent or irreversible changes. The risks and benefits are discussed and an individualised care plan agreed. We often use low-dose oestrogen therapy to start with, but over time and depending on a client's goals and progress on treatment, standard-dose oestrogen therapy can be

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	considered (in conjunction with the gender specialists in the core team). Additionally, anti-androgens or GnRH analogues may also be used depending on a client's individualised goals and progress on treatment [1].
Duration of treatment	Testosterone: long term Progestins or GnRH analogues (if they were necessary to suppress cycling): until genital surgery or oophorectomy
Criteria for stopping treatment	**Preoperative** Significant side effects / lack of response at adequate doses / client self-discharges from the GIC **Postoperative** Development of significant contraindication to testosterone use
Monitoring Requirements before Starting Treatment:	**Gender Clinicians:** Psychological / psychiatric assessment of client's suitability for treatment. Diagnosis of gender incongruence. Assessment of the individual's ability to consent to treatment. Screening for self-administered substances. Review of baseline screening blood tests and information once received from GP (as per below). **GP:** Organise **baseline tests, with blood tests taken as a fasting sample and in the follicular phase days 2-8 of the menstrual cycle (where possible)**, as follows: • Blood tests: FSH, LH, Oestradiol, Testosterone, Prolactin, SHBG, Vitamin D, Liver function, Fasting glucose or Hba1c, Fasting lipids, Full blood count • Blood pressure and Height, Weight, BMI Please **send those results to** GIC.Endo@tavi-port.nhs.uk for review, along with a **general medical summary** and **medication list**
Monitoring requirements once stable, including frequency:	**Consultant/Gender Nurse Specialist:** to advise GP on dose alterations required based on hormone and other monitoring information provided. **GP:** Measure the following 8 weeks after any adjustment to testosterone gel therapy, or at the 4th injection if changes are made to Sustanon/Testosterone Enantate therapy, or at the 3rd injection if making changes to Nebido injections. Additionally, monitoring should be done every 3-6 months in the first year of therapy, every 6-12 months in the second year, and then annually thereafter if therapy is stable.

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	• Testosterone • Full blood count • Liver function tests • Fasting lipids • BMI, blood pressure For non-binary patients, a DEXA scan 3 years after initiation of low-dose testosterone treatment for bone assessment.
Follow up arrangements **and** **Prescribing Responsibilities:**	**Gender Clinicians:** • Clients will be reviewed by the GIC at regular intervals. • The specialist team will take responsibility for the recommendation of treatment, counselling about risks and benefits of therapy, and take responsibility for recommending alterations to GPs until client is stabilised on therapy • To oversee the whole programme of assessment and treatment, including dose adjustment as necessary to reach a maintenance level • To advise GP on any problems arising from treatment which may need a dose adjustment or a change in medication. **GP :** • The GP will take on prescribing as per the shared care agreement, with the support and guidance of the GIC • The GP will be responsible for the ongoing prescribing of testosterone and ovarian inhibitors and will continue to act as the primary contact for general healthcare. • GP to refer to specialist team if any significant developments or deterioration occur, such as occurrence of side-effects, worsening of symptoms or complications of hormone therapy. • The GP to take advice of surgeons on pausing and restarting hormones in relation to genital reconstructive surgery. • Following discharge from the service the GP will follow the discharge guidance provided by the specialist service and maintain the prescription of the patient's hormone therapies. The GP will contact the specialist service if there are any complications that arise or if there are significant changes in the patient's gender situation and gain further advice from the specialist service. **Gender Nurse Specialist:** The Gender Nurse Specialist will provide support and advice for General Practitioners, Community Pharmacists, District Nurses, and the client on request.
Management of complications on hormone therapy	<u>1. Abnormal Liver Function Tests:</u> For values less than 3x the upper limit of normal: check medicines and alcohol history and re-test in 4-6 weeks. If Liver function tests are abnormal on repeat, then perform further investigations to determine the cause:

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	Hepatitis B and C serology, HIV serology, EBV, Ferritin, Copper, Caeruloplasmin, liver auto-immune screen, ultrasound of the liver. If the person is using injectable testosterone it may be appropriate to change to a topical testosterone gel to reduce the strain on the liver; please discuss this with the GIC team. If values are greater than 3x the upper limit of normal: GP to temporarily suspend hormone therapy and refer to local hepatology. <u>2. Lipids:</u> Normal cardiovascular risk assessment and management applies. Seek advice if significant changes in lipids. Calculate the Q-risk score of the patient using the male gender to make intervention decisions. For individuals with an LDL over 4.9 mmol/L, as per NHS England guidance [18], we recommend lifestyle and dietary advice and a repeat blood test which includes fasted lipid profile and LipA. If LipA is above normal range, TC > 9.0 nmol/l, LDL-C > 6.5 mmol/l, and non-hdl-c > 7.6 mmol/l referral to specialist lipid clinic is recommended. <u>3. Polycythaemia: actions for Haematocrit / Packed Cell Volume levels:</u> •Haematocrit less than 0.52 is acceptable. •Haematocrit 0.52 – 0.55: Advise patient to drink 2L water, ensure they are not smoking. Repeat bloods just before next Sustanon or Nebido injection, or 8 weeks later if using gel. If still raised on repeat, GP to seek advice from GIC. •Haematocrit 0.55 – 0.59: GP to inform GIC urgently. Check FBC history to see if a pattern. Advise patient to drink 2L water, ensure they are not smoking. Repeat bloods just before next Sustanon or Nebido injection, or 8 weeks later if using gel. If pattern of polycythaemia on injections, then we advise switching to testosterone gel (as above) and also assess for other potential causes such as Obstructive Sleep Apnoea. •Haematocrit 0.60 or above: GP to pause testosterone therapy and refer urgently to haematology for venesection, also inform GIC urgently. After haematology clearance then return to testosterone as topical therapy, with haematology plan for venesection. If stopping therapy, reassure the patient that this is temporary, and that we would expect testosterone therapy to be resumed after the pause in treatment. The pause is unlikely to cause significant change in physical appearance. <u>4. New diagnosis of Cancer, Stroke or Myocardial Infarction:</u> Temporarily suspend hormone therapy until discussion with the GIC team.
Practical issues including other relevant advice/information:	The side effect profile and safety is identical to that seen in cisgender males having testosterone replacement for hypogonadism. The only difference in trans men is the need to monitor the effects of testosterone on the genital tract and uterus, based on symptoms.

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Medication information, particularly in relation to potential interactions, can be found in the latest edition of the BNF	**Polycythaemia** Testosterone replacement can be associated with polycythaemia, and this increase in blood viscosity can lead to an increased incidence of stroke. In those that have a raised haematocrit there appears to be an increased risk of stroke[8]. This can occur even in young subjects, as both stroke and myocardial infarction have been reported in athletes that abuse testosterone[9]. Polycythaemia is seen more when injectable testosterone is used and appears to be proportional to the amount of supraphysiological testosterone that is administered. For this reason the aim of treatment is to keep the peak testosterone within the upper normal male range but less than 30 nmol/l whilst keeping the trough level at the bottom of the normal male range (8-12nmol/l). Polycythaemia is seen much less with other formulations. Polycythaemia usually responds to a decrease in the dose of testosterone, especially if this is changed to a non-injectable formulation. When this is inadequate, regular venesection to bring the haematocrit down into the normal range can be instituted, and this allows the testosterone therapy to be continued. The frequency of the venesection is variable, but in this situation often needs to be performed 4-6 weekly to control the haematocrit. **Liver Dysfunction** Anabolic steroids are no longer used in routine testosterone replacement and so the incidence of hepatic dysfunction associated with testosterones use has reduced. In one series, however, transient increases in liver function enzymes was seen in 4.4% of trans men and this was prolonged (>6months) in 6.8%[10]. LFT abnormalities are usually minor and do not require cessation of treatment. Routine monitoring of the liver function in clients on testosterone replacement is recommended. Minor derangement of liver function, with increases in liver enzyme levels to less than three times the upper limit of normal do not require suspension of testosterone therapy. Advice should be sought on deranged liver function. Screening for other causes of hepatic dysfunction should be performed and ultrasound scanning of the liver, to exclude any hepatic lesion or the presence of gallstones. There have been no reports of liver tumours with testosterone esters. **Lipid Profile** The administration of testosterone in trans men is associated with an increase in triglycerides and a decrease in plasma HDL levels, both of which are proatherogenic. However, total cholesterol and LDL cholesterol levels remain unchanged[11]. **Cardiovascular disease** The cardiovascular risk of transgender men that does not appear to be any higher than the cisgender male population. The majority of studies has shown that cardiovascular risk is lower than the cisgender population(10, 12). One study has suggested that the myocardial infarction risk was

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similar to the cisgender male population but this is not a typical finding(13). Meta analysis however emphasises the importance of additional CV risk factors such as smoking, reduced exercise, diabetes, and non-Caucasian ethnic origin, all of which were seen in higher numbers in the transgender population(14)
Cardiovascular risk may be increased compared with cisgender females. A recent meta-analysis suggested that the relative risk of myocardial infarction was 1.7 [95% CI 0.8–3.6] compared to cisgender females(15).

Endometrial Hyperplasia and Gynaecological Malignancy

Testosterone can be aromatised to oestradiol. Exposure to high levels of unopposed oestradiol (in the absences of progesterone) is associated with endometrial hyperplasia and endometrial cancer in cisgender women. This occurs more commonly in cisgender women who are obese or who have polycystic ovarian syndrome (PCOS) [19, 20, 21, 22]. One small study reported risk of endometrial hyperplasia is 15% in trans men [16]. It did not report the number of cases that had endometrial hyperplasia *with atypia* which is the associated with progression to cancer. However, this study raised the concern that theoretically, in the longer term, there could be an increased risk of endometrial cancer. However, subsequent evidence regarding frequency of endometrial hyperplasia with atypia and endometrial cancer in trans men, has been reassuring [23]. In our practice the incidence of endometrial hyperplasia is much lower than 15%.

No routine monitoring of the endometrial thickness by ultrasound scanning is recommended, as there is no evidence to support this in other groups who do have proven risk e.g. cisgender women with PCOS.

It is also worth noting that after about 6 months on testosterone therapy the ovaries may take on a polycystic appearance.

Importantly, if irregular genital bleeding occurs then the client should undergo gynaecological examination and ultrasound scanning +/- endometrial biopsy to rule out any neoplastic alteration in the endometrial epithelium. Again, this draws parity with PCOS.

Genital atrophy

When the ovary is suppressed and oestradiol is not produced there can be symptoms of genital atrophy which can result in genital dryness, genital irritation and contact bleeding after sexual activity.

This can be treated using standard treatments for postmenopausal genital atrophy which would include topical oestrogen preparations such as Vagifem, Ovestin or alternatively selective oestrogen receptor modulators such as Ospemifene 60 mg once a day.

Scalp hair loss

In those that are genetically programmed to undergo androgenic alopecia, testosterone therapy can result in significant scalp hair loss. Treatments that can be of use include topical Minoxidil 5% solution oral minoxidil or in some cases 5 alpha reductase inhibition with finasteride or dutasteride.

Minoxidil can be purchased as an over-the-counter preparation however the use of 5 alpha reductase inhibitors in this situation should be

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recommended by the gender specialist as it may impact on the effectiveness of the testosterone treatment which the gender specialist team should give advice to the individual.

Obstructive Sleep Apnoea
Testosterone therapy exacerbates the symptoms of obstructive sleep apnoea. In a trans man who has symptoms of obstructive sleep apnoea, symptom scores should be assessed and referral made to a specialist in sleep disorders for treatment if the client displays any deterioration in their condition.

Fertility and contraception
Testosterone therapy leads to a suppression of gonadotrophin production and subsequent reduction in ovulation. Clients are counselled that treatment will reduce their fertility. The effects of hormone treatment on fertility are usually reversible however there may be a permanent reduction in fertility potential. Fertility preservation is discussed with clients before they start on hormone treatment and, if desired, they should be referred for fertility preservation through local fertility services before commencing on hormone treatment.

With regards to contraception, hormone therapy cannot be relied upon as effective contraception. The usual recommendation is that any of the progesterone-based contraceptives may be used. Choosing a preparation that does not cause irregular genital bleeding is usually preferrable as irregular genital bleeding may trigger significant dysphoria in transgender men and transmasculine people.

Reliable contraception is important as testosterone may be teratogenic. Parenteral methods such as progesterone implants, progesterone injections, or an intrauterine device (ideally hormone-eluting to suppress the endometrium) in addition to progesterone-only oral contraception may be used.

Pregnancy and lactation
Testosterone therapy is contraindicated in pregnancy and lactation. It should be stopped before pregnancy is achieved. If a person becomes pregnant on testosterone therapy, kindly discontinue testosterone therapy immediately and seek advice from your local obstetrics service and the GIC.
For further advice on reinitiating of testosterone therapy postpartum please contact the GIC.

Bone Health

We know that standard hormone therapy aimed at physiological replacement maintains bone mineralisation in transgender men. Routine monitoring of bone mineralisation is therefore not required unless there are specific risk factors for osteoporosis.

Monitoring of bone health is not routinely required unless the person has significant risk factors for osteoporosis or has had a significant break from sex steroid treatment (>24 months). The GIC clinician will make a recommendation about DEXA scanning but the performance of that scan would be deferred to primary care.

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	For non-binary people we do not have the same outcome data. We therefore suggest that in our monitoring of bone health by DEXA scanning is done 3 years after initiation of low-dose testosterone therapy if oestradiol production is suppressed. **Renal impairment** Some studies suggest that testosterone therapy may increase proteinuria (protein in the urine). However, this is more common in individuals with pre-existing kidney disease [24]. Testosterone is metabolized in the liver and cleared by the kidneys. In individuals with renal impairment, this clearance could be reduced, leading to elevated levels of free testosterone in the blood [25]. There are no specific guidelines focused solely on kidney function in transgender men using testosterone. We don't routinely recommend adjustments to treatment in cases of mild renal impairment, but advice regular monitoring of renal function. This includes monitoring blood pressure, urinary protein levels and Kidney function tests/GFR [1]. In cases of moderate to severe impairment, kindly consult the GIC. **National Screening Programmes:** There is a comprehensive document on the gov.uk website: https://www.gov.uk/government/publications/nhs-population-screening-information-for-transgender-people The client should be advised that they will get an automatic call-up to male but not female screening if they have had their gender changed on the NHS computer system. They will need to remember to access screening such as cervical smears (if have not had hysterectomy) and mammography. Breast checking must still be done after chest reconstructive surgery as some breast tissue does remain. A more nuanced discussion of recommended screening navigating this as a transgender person can be found at: https://outpatients.org.uk/tnbgd-screening/
Information provided	Clients are given a copy of the clinic's Hormone Management Booklet which is also available for GPs on our website or GPs can request it by email at gic.endo@tavi-port.nhs.uk. It is based on The Transgender Handbook: A Guide for Transgender People, Their Families and Professionals (17)

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Gender Identity Clinic contacts:

GIC Clinic Web Site **www.gic.nhs.uk** GIC phone number: 0208 938 7590

Email: hormone therapy related queries can be sent to gic.endo@tavi-port.nhs.uk (other queries will be forwarded to the most appropriate clinician or dealt with by the administrative team, as appropriate).

GP hormone advice line: [redacted] (this line is for GPs/healthcare professionals only with questions about hormone therapy)

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REFERENCES

Evidence Base for treatment and Key references:

1. Coleman E, Radix AE, Bouman WP, Brown GR, de Vries ALC, Deutsch MB, et al. Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. *Int J Transgend Health.* 2022;23(Suppl 1):S1-S259.
2. D'hoore L, and T'Sjoen G. Gender-affirming hormone therapy: An updated literature review with an eye on the future. *J Intern Med.* 2022;291(5):574-92.
3. Seal LJ. In: Bouman WPA, Jon ed. *The transgender handbook : a guide for transgender people, their families and professionals*. New York: Nova Publishers; 2017:227-49.
4. Seal LJ. A review of the physical and metabolic effects of cross-sex hormonal therapy in the treatment of gender dysphoria. *Ann Clin Biochem.* 2016;53(Pt 1):10-20.
5. Nota NM, Wiepjes CM, de Blok CJM, Gooren LJG, Kreukels BPC, and den Heijer M. The Occurrence of Acute Cardiovascular Events in Transgender Individuals Receiving Hormone Therapy: Results from a Large Cohort Study. *Circulation.* 2019.
6. J SL. Testosterone Replacement Therapy. *Medicine International.* 2009;37(9):445-9.
7. Barrett JD. *Transsexual and other disorders of gender identity : a practical guide to management.* Abingdon: Radcliffe; 2007.
8. Krauss DJ, Taub HA, Lantinga LJ, Dunsky MH, and Kelly CM. Risks of blood volume changes in hypogonadal men treated with testosterone enanthate for erectile impotence. *J Urol.* 1991;146(6):1566-70.
9. Ferenchick GS. Anabolic/androgenic steroid abuse and thrombosis: is there a connection? *Med Hypotheses.* 1991;35(1):27-31.
10. van Kesteren PJ, Asscheman H, Megens JA, and Gooren LJ. Mortality and morbidity in transsexual subjects treated with cross-sex hormones. *Clin Endocrinol (Oxf).* 1997;47(3):337-42.
11. Elbers JM, Giltay EJ, Teerlink T, Scheffer PG, Asscheman H, Seidell JC, et al. Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. *Clin Endocrinol (Oxf).* 2003;58(5):562-71.
12. Asscheman H, Giltay EJ, Megens JA, de Ronde WP, van Trotsenburg MA, and Gooren LJ. A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. *Eur J Endocrinol.* 2011;164(4):635-42.
13. Nota NM, Wiepjes CM, de Blok CJM, Gooren LJG, Kreukels BPC, and den Heijer M. Occurrence of Acute Cardiovascular Events in Transgender Individuals Receiving Hormone Therapy. *Circulation.* 2019;139(11):1461-2.
14. Aranda G, Halperin I, Gomez-Gil E, Hanzu FA, Seguí N, Guillamon A, et al. Cardiovascular Risk Associated With Gender Affirming Hormone Therapy in Transgender Population. *Front Endocrinol (Lausanne).* 2021;12:718200.
15. van Zijverden LM, Wiepjes CM, van Diemen JJK, Thijs A, and den Heijer M. Cardiovascular disease in transgender people: a systematic review and meta-analysis. *Eur J Endocrinol.* 2024;190(2):S13-S24.
16. Futterweit W. Endocrine therapy of transsexualism and potential complications of long-term treatment. *Arch Sex Behav.* 1998;27(2):209-26.

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17. Seal L, J. In: Bouman WP, and Arcelus J eds. *The Transgender Handbook: A Guide for Transgender People, Their Families and Professionals*. New York: Nova Science Publishers; 2017.
18. Simon Broome or Dutch Lipid Clinic Network (DLCN) criteria to make a clinical diagnosis of FH can also be used. www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/04/lipid-management-pathway-v6.pdf
19. Allen NE, Key TJ, Dossus L, Rinaldi S, Cust A, Lukanova A, et al. Endogenous sex hormones and endometrial cancer risk in women in the European Prospective Investigation into Cancer and Nutrition (EPIC). Endocr Relat Cancer. 2008;15(2):485-97.

20. Rosenfield RL, Ehrmann DA. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev. 2016;37(5):467-520.

21. Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril. 2018;110(3):364-79.

22. Fearnley EJ, Marquart L, Spurdle AB, Weinstein P, Webb PM. Polycystic ovary syndrome increases the risk of endometrial cancer in women aged less than 50 years: an Australian case-control study. Cancer Causes Control. 2010;21(12):2303-8.
23. Ralph O, Shroff N, Christopher N, Ahmed A, Berner A, Barrett J, et al. RESPONSE OF ENDOMETRIUM TO TESTOSTERONE THERAPY IN TRANS MEN AND NON-BINARY PEOPLE UNDERGOING HYSTERECTOMY. Journal of Urology. 2019;201(4):E866-E7.

24. Zhou, L., et al. (2018). The Relationship Between Testosterone and Proteinuria in Transgender Men: A Cross-Sectional Study. *Nephrology Dialysis Transplantation*, 33(8), 1354-1361.
25. an der Linde, H. et al. (2020). Renal Implications of Hormone Therapy in Transgender Individuals: A Focus on Testosterone. *Endocrine Reviews*, 41(6), 615-625

NB: for full details of adverse effects and drug interactions refer to latest Summary of Product Characteristics https://www.medicines.org.uk/emc/

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SHARED CARE PRESCRIBING AGREEMENT

(Appendix ia)

CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- The GIC clinicians will establish that the person is suitable for hormone treatment when they are in a stable social and psychological circumstance.
- The GIC clinicians will establish that there is no significant medical or endocrinological contraindication to hormone therapy.
- The GIC clinicians will request that the GP commence prescribing when these conditions are met.
- The GIC clinicians will be available to give advice on further management.

AREAS OF RESPONSIBILITY

Specialist Gender Identity Clinic Team/Consultant Responsibilities

- Establish or confirm diagnosis and assess client suitability for treatment
- Assessment of baseline bloods , and monitoring bloods until stable by GIC Endocrine Team
- Discuss treatment with client and ensure they have a clear understanding of benefits and side-effects of treatment, including dose adjustments and how to report any unexpected symptoms
  The specialist team provides the client with information and advice, supported by a written information booklet
- Obtain signed consent for hormonal treatment
- Send a signed shared care guideline with client details completed together with relevant clinical information to GP
- Contact GP directly if response to shared care request has not been received within two weeks
- Monitor treatment according to clinical guidance and advise client and GP on dose titration of medicines.

Ongoing Care Arrangements: Specialist Team to

- Write to GP following clinic contacts and inform GP when client is stable on hormones.
- Inform GP of abnormal monitoring results and any recommended changes in therapy prescribed by the GP, including the need to discontinue if appropriate
- Evaluate adverse events reported by GP or client and communicate outcome to GP
- Make arrangements for ongoing monitoring and follow up according to shared care guidelines including continued need for therapy.

Gender Specialist Nurse:
The Gender Specialist Nurse will provide support and advice for General Practitioners, Community Pharmacists, District Nurses on request.

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GP RESPONSIBILITIES
▪ Consider shared care proposal and if in agreement to respond within two weeks of receipt ▪ If do not agree to shared care, discuss with requesting consultant or local CCG medicines management team, within two weeks of receipt of shared care request ***After agreement to share care*** ▪ Prescribe and monitor treatment as advised by the specialist team and according to shared care guideline ▪ Monitor general health of client and check adverse effects as appropriate; ensure client is aware of warning symptoms and how to report them ▪ Inform specialist team of suspected adverse effects and report via yellow card scheme if necessary ▪ Stop treatment on advice of specialist team or immediately if urgent need arises ▪ Check compatibility interactions when prescribing new or stopping existing medication ▪ Discuss any abnormal results with specialist consultant and agree any action required ▪ Take advice from surgical teams about pausing and restarting therapy in relation to genital reconstructive surgery. Only ask specialist to take back prescribing should unmanageable problems arise. Allow an adequate notice period.
CLIENT'S RESPONSIBILITIES
▪ Keep a copy of information provided by Gender Identity Clinic, including consent to treatment, to take along when seeing GP ▪ Take medicines as agreed and prescribed ▪ Report any adverse effects to GP or hospital doctor at the earliest opportunity ▪ Ensure that you attend for tests as requested by your Gender Clinician or GP ▪ Do not share medicines ▪ Attend appointments for review as necessary ▪ Always inform the specialist team and GP of all medication being taken, whether prescribed or bought

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SHARED CARE PRESCRIBING AGREEMENT

(Appendix ib)

GENDER CLINICIAN

Client name:

Client ID:

Client NHS No:

Date of Birth:

☐ I confirm that I have assessed the above named individual and it is my clinical recommendation that the following treatment is prescribed:

☐ Furthermore, the "Areas of Responsibility" have been covered and I agree to the "follow-up arrangements".

Signature:

Print Name:

Date:

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CLIENT CONSENT LETTER FOR INITIATION OF HORMONES

(Appendix ii)

I, …… (print name) met with the above named clinician.

☐ I can confirm that I am aware of the potential effects, side effects and expectations of hormone therapy. In addition I am also aware of the potential effects that this therapy will likely have on my fertility. I do not wish to discuss this further with another medical doctor.

☐ Furthermore I confirm that I will adhere to the "Client Responsibilities" as outlined in the shared care agreement.

…… (signature) Date: ……..

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SHARED CARE PRESCRIBING AGREEMENT

(Appendix iii)

GP/Primary Care Provider

Client name:

Client ID:

Client NHS No:

Date of Birth:

☐ I confirm that I have read the shared care prescribing agreement and agree to the "Areas of Responsibility". As in shared care arrangements with other specialist services, and as is consistent with NHS England and GMC guidance, I understand that this includes prescribing and monitoring the recommended treatment as outlined in this shared care document, with the support and advice of the specialist gender service.

Signature:

Print Name:

Date:

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