SHARED CARE PRESCRIBING GUIDANCE FOR

Treatment of Gender Dysphoria In People Assigned Female at Birth Transitioning to a Masculine Gender Identity

Applicable to:	GPs referring clients to the Charing Cross Gender Identity Clinic
Date Approved:	28 April 2022
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INTRODUCTION

This document has been prepared by Dr Leighton Seal, 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.

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) to suppress oestrogen 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. The standardised mortality rate for trans men is 1.0, demonstrating that longer term testosterone therapy is not detrimental or harmful. That is to say, clients are no more likely to die as a result of taking this treatment than if the GP did not prescribe at all.

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.

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,

Dr James Barrett
Clinical Director, Gender Identity Clinic

Dr Leighton Seal
Consultant Endocrinologist

Treatment of Gender Dysphoria in Trans Masculine People

CLINICAL INFORMATION

Indication(s):	Treatment of gender dysphoria following psychological assessment at Gender Identity Clinic.
Place in Therapy:	Hormonal therapy will usually be recommended after the client has been assessed by 1-2 mental health practitioners (MHP) following a period of assessment by them. This is consistent with the Royal College of Psychiatrists Joint Society guidelines. Usually the client lives in their preferred gender role full-time for a period, which is not usually less than three months, prior to the initiation of hormone therapy. This will be adhered to in the vast majority of cases. Commencement of hormonal therapy should generally be deferred until the client has demonstrated consolidation of their gender identity through social transition, and they have made progress in mastering the challenges that their new social role has brought. 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 30 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.[1.2] Indeed Sustanon is licensed as supportive therapy for trans men.
Dose & route of administration:	**Testosterone to cause masculinisation:** **First line:** **<u>Injectable Testosterone:</u>** Sustanon 250 mg (IM) 4 weekly. Testosterone Enantate can be seen as equivalent. Sustanon should not be used in clients with nut allergy. Doses of short acting testosterone preparations at 250 mg 2-4 weekly are usually adequate to suppress menstruation, and the aim of therapy is to achieve trough testosterone levels at the bottom of the normal male range (10-12 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 (25-30 nmol/l) one week after the injection. Monitoring should be performed in the steady state, at the time of the 4th injection. Both the trough and peak testosterone levels need to be measured. Titration of the trough value is achieved by varying the length of time between the injections, by weekly intervals [(2)]. Titration of the peak value is achieved by varying the dose administered with each injection, by 50 mg each time. Focus on the trough level first. If both trough and peak levels are too high it is best to adjust the dosing frequency first and then the dose. **Second line:** **<u>Topical gel preparations, dose range 20-100 mg</u>**

Testogel 16.2 mg/g gel
Tostran 2% gel
Testavan 20 mg/g gel

The usual starting dose is 40 mg daily:
2 squirts of Testogel 16.2 mg/g (= 40.5 mg)
4 squirts of Tostran 2% (= 40 mg)
2 squirts of Testavan 20 mg/g (= 46 mg)

The levels are then titrated to achieve a plasma testosterone in the middle adult range 15-20 nmol/l.

The level should be measured 4-6 hours after the gel application and there should be no gel applied to the arm on that day[2].

With gels, care must be taken to avoid transfer to other humans and to animals.

Third Line:
Long acting injectable testosterone:
In cases where the short-acting injection causes 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[2].

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:

Nebido Loading:

As per the information leaflet, Nebido must be administered by a trained healthcare professional, as a deep IM injection over 2 minutes.

Stage One:

Nebido 1000mg IM 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)

Stage Two:

Six weeks later a Nebido 1000mg intramuscular

Stage Three:

Six weeks later a Nebido 1000mg intramuscular

This completes the loading phase.

Stage Four:
The next Nebido 1000mg is given **12 weeks** later, with bloods taken prior:

Blood monitoring:
Take trough bloods prior to the first 12 week administration of Nebido

	for: testosterone, FBC, LFTs, fasting lipids. Once you have those results please send to the Gender Identity Clinic **Stage Five:** Nebido 1000mg intramuscular every 12 weeks. **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 [3] **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)
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:	**Consultant/Gender Specialist** Psychiatric assessment of client's suitability for treatment. Screening for self-administered substances Measurement of LH, FSH, testosterone, oestradiol, SHBG, prolactin, lipid profile, LFTs, glucose, vitamin D, FBC, (and renal function if indicated)
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 every 3–6 months initially, annually thereafter: Testosterone, FBC, LFTs, fasting lipids,

	BMI
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. **Gender Nurse Specialist:** The Gender Nurse Specialist will provide support and advice for General Practitioners, Community Pharmacists, District Nurses, and the client on request.
Practical issues including other relevant advice/information: **Medication information, particularly in relation to potential interactions, can be found in the latest edition of the BNF**	The side effect profile and safety is identical to that seen in genetic males having testosterone replacement for hypogonadism. The only difference in trans men is the need to monitor the effects of testosterone on the uterus every two years or until the client undergoes hysterectomy. <u>1. Polycythaemia</u> 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 haematocrit above 48% there appears to be an increased risk of stroke[4]. This can occur even in young subjects, as both stroke and myocardial infarction have been reported in athletes that abuse testosterone[5]. 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 i.e. 25-30 nmol/l whilst keeping the trough level at the bottom of the normal male range (10-12nmol/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.

2.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%[6].

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.

3. 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[7]. It is interesting that these changes in lipid profile do not appear to translate into an alteration in cardiovascular risk, as there is no increase in cardiovascular mortality in treated trans men; indeed the myocardial infarction rate is approximately half that expected in the general male population[8].

4. Gynaecological Malignancy
Testosterone can be aromatised to oestradiol. The reported risk of endometrial hyperplasia is 15% in trans men [9]. Monitoring of the endometrial thickness by ultrasound scanning every two years is recommended. It is our usual practice to recommend hysterectomy after two years of testosterone therapy but if the client does not wish to do this then ongoing ultrasound scanning will be needed. If irregular bleeding occurs then the client should undergo ultrasound scanning and endometrial biopsy to rule out any neoplastic alteration in the endometrial epithelium.

5.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.

6. Monitoring of bone health

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.

7. 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.
Information provided	Clients are given a copy of the clinic's Hormone Management Booklet which is also available for GPs via emailing the gender nurse specialist at gic.noreply@nhs.net or by faxing or writing in to request a copy. It is based on The Practical Management of Hormonal Treatment in Adults with Gender Dysphoria[13]**.**

COMMUNICATION AND SUPPORT

Gender Identity Clinic contacts:

GIC Clinic Web Site **www.gic.nhs.uk**

GIC number: 0208 938 7590; Fax 0208 181 4506

Email gic.noreply@nhs.net (this is forwarded to either the Endocrine Team or the most appropriate clinician)

GP hormone advice line: 020 8938 7369 (this line is for GPs only with questions about hormone therapy)

REFERENCES

Evidence Base for treatment and Key references:	1. 2012. Electronic Medicines Compendium. https://www.medicines.org.uk/emc/product/5373#INDICATIONS 2. J, S.L. 2009. Testosterone Replacement Therapy. *Medicine International* 37:445-449. 3. Barrett, J.D. 2007. *Transsexual and other disorders of gender identity : a practical guide to management*. Abingdon: Radcliffe. xii, 298 p., [298] p. of plates pp. 4. Krauss, D.J., Taub, H.A., Lantinga, L.J., Dunsky, M.H., and Kelly, C.M. 1991. Risks of blood volume changes in hypogonadal men treated with testosterone enanthate for erectile impotence. *J Urol* 146:1566-1570. 5. Ferenchick, G.S. 1991. Anabolic/androgenic steroid abuse and thrombosis: is there a connection? *Med Hypotheses* 35:27-31. 6. van Kesteren, P.J., Asscheman, H., Megens, J.A., and Gooren, L.J. 1997. Mortality and morbidity in transsexual subjects treated with cross-sex hormones. *Clin Endocrinol (Oxf)* 47:337-342. 7. Elbers, J.M., Giltay, E.J., Teerlink, T., Scheffer, P.G., Asscheman, H., Seidell, J.C., and Gooren, L.J. 2003. Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. *Clin Endocrinol (Oxf)* 58:562-571. 8. Asscheman, H., Gooren, L.J., and Eklund, P.L. 1989. Mortality and morbidity in transsexual patients with cross-gender hormone treatment. *Metabolism* 38:869-873. 9. Futterweit, W. 1998. Endocrine therapy of transsexualism and potential complications of long-term treatment. *Arch Sex Behav* 27:209-226.

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

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.

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 also 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

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:

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: ……..

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: