Lothian NHS Board

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Date 29/01/2025
Our Ref 9561

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Dear

FREEDOM OF INFORMATION – SHARED CARED PROTOCOL

I write in response to your request for information in relation to shared care protocols.

Question:

- Under the freedom of Information Act (Scotland) 2002, and in response this is FOI

  https://www.whatdotheyknow.com/request/gp_protocol_for_transgender_care#incoming-2692262

  I would like to request a copy of the shared cared protocol between the Chalmers clinic and GPs that is referred to in the attached FOI.

Answer:

Please see enclosed.

I hope the information provided helps with your request.

If you are unhappy with our response to your request, you do have the right to request us to review it. Your request should be made within 40 working days of receipt of this letter, and we will reply within 20 working days of receipt. If our decision is unchanged following a review and you remain dissatisfied with this, you then have the right to make a formal complaint to the Scottish Information Commissioner within 6 months of receipt of our review response. You can do this by using the Scottish Information Commissioner's Office online appeals service at www.itspublicknowledge.info/Appeal. If you remain dissatisfied with the Commissioner's response you then have the option to appeal to the Court of Session on a point of law.

If you require a review of our decision to be carried out, please write to the FOI Reviewer at the email address at the head of this letter. The review will be undertaken by a Reviewer who was not involved in the original decision-making process.

FOI responses (subject to redaction of personal information) may appear on NHS Lothian's Freedom of Information website at: https://org.nhslothian.scot/FOI/Pages/default.aspx

Yours sincerely

ALISON MACDONALD
Executive Director, Nursing
Cc: Chief Executive
Enc.

SHARED CARE AGREEMENT

Name of medicine	*Feminising Endocrine Treatment (Estradiol and GnRHa)*
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 to establish treatment and then recommend prescribing for all those seeking feminising endocrine treatment. GPs will be asked to be undertake the prescribing and reporting of any issues to the GIC from the commencement of treatment.

However, recall and monitoring (including phlebotomy and blood pressure measurement) will be undertaken by the GIC, who will also arrange any clinical review required. The GP will then be asked to prescribe accordingly. This has now been agreed with the Lothian GP Sub-Committee.

This document uses the term **trans women** to include trans women and non-binary people (recorded male at birth) using feminising hormones in connection with gender dysphoria or incongruence.

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 recommending initiation of treatment (communicated to GP to prescribe). This will include consent for the unlicensed use of medications
- Provide information both to the GP and the patient outlining risks of treatment
- Monitoring for the first year (or until patient is on a stable medication regimen)
- Communication with the GP about any changes in treatment
- Referral for specialist interventions relating to gender reassignment and transitioning
- Referral for non-specialist interventions suggested by the GIC (e.g. CMHT, weight management etc)
- Advise about changes in CHI, breast cancer screening, prostate awareness and over-65 Abdominal Aortic Aneurysm screening – details available from national screening programmes
- Assess cardiovascular risk status (ASSIGN score) and advise appropriately. The literature suggests that the cardiovascular risks are those of untreated non transgender men, so the GIC recommendation is to use male gender in the risk calculation
- Assess thrombo-embolic risk and advise appropriately
- 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 patient will be offered a review, every 1-2 years depending on level of clinical risk. 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.

The following will be organised by the GIC, with a recall system, to monitor ongoing hormonal therapy treatments:

- Maintain awareness of prostatic disease and institute appropriate investigations if lower urinary tract symptoms occur
- Undertake any BP measurements or blood tests required, review clinically as indicated by the patient's situation and risk and write to the GP to advise appropriate prescribing following this
- Check at review that the patient has not developed key conditions that would change hormonal prescribing - see monitoring summary.

General Practitioners and primary care non-medical prescribers

- Be aware of the potential for prostatic disease and institute appropriate investigations if lower urinary tract symptoms occur. Note that PSA monitoring is not required
- Institute changes in treatment as per GIC advice following review. If the patient does not attend necessary reviews, the GP will be informed and prescribing reviewed
- Inform the GIC
    - for risk re-evaluation for new diagnoses of cerebrovascular disease, coronary heart disease or venous thrombo-embolism
    - if new diagnosis of active liver disease or liver tumours

There will be a very small number of high-risk patients whose care – including prescribing - should be solely undertaken by the specialist service.

THERE IS A SUMMARY OF MONITORING REQUIREMENTS AT THE END OF THIS DOCUMENT.

Please note that for patients aged under 40 (the vast majority), unless there is a significant new diagnosis, the only monitoring requirement is for periodic BP and smoking advice. The only exception is the (very rare) patient on spironolactone or cyproterone.

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). 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 available at NSD_GRP_OG_05-Endocrine-and-fertility-preservation-guidance-2022-v0.8.pdf (scot.nhs.uk)

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 and use of feminising endocrine treatment for gender dysphoria.

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 available at Endocrinology Guidance (scot.nhs.uk). 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.

Oestrogen evidence base in non transgender women

The risks of exogenous oestrogen have been investigated in large studies of HRT in non transgender women, although this remains a debated area. The impact of age is however very important: for younger patients, the equivalent patient group would be women with premature ovarian insufficiency, but the evidence regarding risk in this group is very limited[i].

The oestrogen doses used for feminising treatment for gender dysphoria are generally higher than those used for HRT, but some of the evidence relating to HRT is likely to have relevance. It is important to note that some HRT risks largely relate to, or are magnified by, combined preparations (ie progestogen-containing) which are not used in trans women. These progestogen-related risks include VTE and breast cancer. Current understanding is that starting oestrogen-only HRT in a healthy 50-year-old woman increases life expectancy, largely related to **reduced** risk of cardiovascular disease.

It is however clear that exogenous oestrogen:

- *increases the incidence of venous thrombo-embolism (VTE), particularly with oral preparations, and this risk is dose-dependent*
- *also increases the risk of ischaemic stroke, particularly in older women. The CHD risk is reduced with oestrogen-only HRT in healthy peri/postmenopausal women but rises if combined HRT is started >10 years after the natural menopause*
- *increases the risk of breast cancer.*

For further information on the risks in non transgender women please see the relevant MHRA advice.

Oestrogen evidence base in trans women

The evidence base in trans women is very limited. A retrospective case-controlled study has shown that trans women on hormone therapy had a higher incidence of both VTE and ischaemic stroke[ii]. The risk differences for VTE at 2 and 8 years were 3.4 and 13.7 relative to non-transgender women on no oestrogen. In contrast to non-transgender women where the VTE risk rises soon after starting treatment, *the risks in the trans women study continued to rise over time*.

There may be an increased risk of MI, and the evidence suggests this, though the estimated risks are the same as those for non-transgender men. Whilst this is a relatively large study in this patient population, very few events were detected, and it was not possible to explore the effects of age or oestrogen dose. Thus, the precision of these risks, and their relevance to younger trans women, particularly with physiological levels of estradiol replacement, remain very unclear.

Older studies are generally poor, because of compounding factors, and that a variety of doses and preparations have been used historically.

Taking the available evidence together:

- *it is very clear that transdermal, rather than oral preparations have the lowest risk of VTE, and that the risk particularly with oral preparations is dose-dependent*
- *That VTE risk is likely raised, and it is also likely that it continues to rise with duration of use*
- *There may be an increased risk of MI (likely similar to non transgender men).*

Indication

Specific to approved use in NHS Lothian (check formulary status)

Dosage and administration

- Transdermal preparations, which avoid first pass metabolism in the liver, are strongly recommended for all patients especially those aged > 40 years and those with higher cardiovascular risk, a high BMI or liver disease. They are associated with reduced VTE risk compared with oral preparations
- Transdermal estradiol patches up to 200 micrograms, changed once or twice weekly according to manufacturer instructions (initial dose titration at CGIC)
- Estradiol gel 0.5mg to 3mg, applied daily
- Oral estradiol 1mg to 6mg daily.

Androgen Suppression

- Leuprorelin/Triptorelin 3/3.75mg 4 weekly or 11.25mg 3 monthly or 22.5mg (triptorelin) 6 monthly by IM injection **OR** Goserelin 3.6mg implant subcutaneously 4 weekly or 10.8 mg implant 3 monthly.

OR

- Cyproterone acetate (25-100 mg daily: 6 monthly checks of LFTs are necessary as serious hepatotoxicity has been reported). This is likely to be used only when patients are already taking it eg prior to moving to Lothian and is rarely prescribed.

Patients may require re-titration of estradiol following gonadectomy, when androgen suppression therapy can be stopped. All should re-engage with the GIC during this period, and the GIC will carry out this titration if indicated.

Estradiol levels up to 600 pmol/L are appropriate though regular screening of estradiol levels is not recommended. The GIC will base its advice regarding changing dose primarily according to clinical response.

Monitoring

There is some internationally recognised guidance for monitoring, but it too has limitations and this guidance reflects a Lothian pragmatic multi-disciplinary consensus view. Many of the recommendations for monitoring come from American practice, often over-interventional in relation to the available evidence. There is 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, overall, the evidence strongly supports the use of interventions in gender dysphoria for better clinical outcomes in consideration of the emotional and psychological risk versus benefit to the patient. Additionally, for patients who have had surgical orchidectomy, exogenous treatment is their only source of sex steroids, which also bring benefits, for bone health for example.

Risks may change over the course of a lifetime and need to be reassessed where new morbidities become apparent. Trans women need to understand that they are at increased risk of the following complications.

1. **Breast cancer**

Trans women taking oestrogen may be at risk of developing breast cancer because of the development of breast tissue. They should be made aware of this, and encouraged to participate in the national breast screening programme and be breast aware.

2. **Venous thrombo-embolism**

Trans women taking oestrogen, and their clinicians, should remain vigilant about the increased risk of VTE, a complication which can happen several years after starting hormone treatment: risks may rise over time. The risk is minimised by taking transdermal oestrogen preparations, and the lowest effective dose.

If someone suffers a venous thromboembolism, oestrogen therapy should be stopped until further assessments are made.

All will be risk-assessed by the GIC at the commencement of treatment, and reviewed periodically by the clinic, but advice should be sought from the GIC, or other relevant specialties, should high-risk situations develop such as:

- Known hereditary or acquired predisposition for venous thromboembolism, such as APC-resistance, (including Factor V Leiden), antithrombin-III-deficiency, protein C deficiency, protein S deficiency
- The presence of multiple risk factors including family history or conditions with a strong association with VTE

Those undergoing major surgery with prolonged immobilisation may need additional prophylaxis.

3. Cardiovascular disease

3.1. The GIC will undertake ongoing cardiovascular risk assessments as outlined below, but all clinicians are encouraged to opportunistically support risk minimisation lifestyle advice:

- **Risk Assessment.** All will have an initial cardiovascular risk assessment (ASSIGN score, using male gender for the risk calculation) at commencement of therapy and be advised accordingly
- **Risk Minimisation.** All should be encouraged to minimise risk through a healthy lifestyle. The standard advice is for: 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/
- **BP and smoking advice – periodic check (annually or biannually):**
- ASSIGN score 5 yearly (age 40-55) and 3 yearly after that to optimise adverse lipid and blood pressure management, using male gender in the risk calculation.

We suggest that:

- Hypertension be treated at the threshold for diabetes or target organ damage. This means active management for those with Stage 1 hypertension and blood pressure readings of: clinic BP≥140/90 (multiple readings) and confirmed by subsequent ABPM daytime average ≥135/85 in keeping with the Lothian Hypertension Guidelines
  - Raised blood pressure: GIC will ask GP to review, undertake further investigation and initiate treatment where required
  - Abnormal lipids and/or elevated ASSIGN score: GIC will ask GP to see patient to discuss management as per local guidance.
- Advice should be sought for those with ASSIGN scores over 20, or hypertension or hyperlipidaemia less than optimally controlled.

3.2. Cardiovascular High-risk situations - Presence or risk of arterial thromboembolism (ATE)

In the following situations, patients will need immediate specialist care or advice:

- Arterial thromboembolism - current arterial thromboembolism, history of arterial thromboembolism (e.g. myocardial infarction) or prodromal condition (e.g. angina pectoris)
- Cerebrovascular disease - current stroke, history of stroke or prodromal condition (e.g. transient ischaemic attack)
- Known hereditary or acquired predisposition for arterial thromboembolism, such as hyperhomocysteinaemia and anti-phospholipid antibodies (anticardiolipin-antibodies, lupus anticoagulant)
- New onset of migraine with focal neurological symptoms.

Urgent advice sought for those with a high risk of arterial thromboembolism due to multiple risk factors (see section 4.4) or to the presence of one serious risk factor such as:

- Diabetes mellitus with vascular symptoms
- Severe hypertension
- Severe dyslipoproteinaemia.

4. The following are NOT required:

- Osteoporosis screening (bone loss only happens with prolonged GnRH treatment without added-in oestrogen, which should not happen)
- Routine measurement of estradiol levels
- Prolactin measurement
- PSA screens
- Screening for meningiomas and prolactinomas (which may be linked to cyproterone acetate usage) as these are exceptionally rare.

Also note that the reference range for some tests will differ from the standard range for that gender. Please see: Laboratory tests with gender-specific reference ranges (excluding hormones).

Test	Frequency	Abnormal result	Action if abnormal result
Creatinine and electrolytes	Annual – ONLY if taking spironolactone		GIC will monitor but for incidental findings, stop medication and seek advice
LFTs	6 monthly – ONLY if on cyproterone		GIC will monitor but for incidental findings, seek advice
BP and smoking advice	Annually or biannually	If hypertensive, treat at threshold for diabetes or target organ damage	Seek advice if severe / poorly controlled hypertension
Cardiovascular risk assessment	See comments above: ASSIGN score 5 yearly (age 40-55) and 3 yearly after that. *Use male gender for risk calculation*	Treat stage 1 hypertension and provide lifestyle advice. Advise of increased risk	The GIC will advise practices if ASSIGN score >20
VTE	Risk assessment at commencement of treatment and if new diagnosis or high-risk situation develops throughout treatment (see section 2 above)		Stop oestrogen and seek immediate advice. Note that VTE is especially associated with oral preparations
New onset active liver disease or malignancy	Throughout duration of treatment	This includes: 1. Presence or history of severe hepatic disease, e.g. active viral hepatitis and severe cirrhosis, as long as liver function values have not returned to normal 2. Presence or history of liver tumours (benign or malignant)	Inform the GIC. Please note that different blood reference ranges may apply and please see Lothian laboratory recommendations
Screening	Advise: breast and abdominal aortic aneurism screening and prostate awareness		NHS Inform provides transgender screening advice

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

[i] ESHRE Guideline Group on POI, Webber L, Davies M, Anderson R, Bartlett J, Braat D, Cartwright B, Cifkova R, de Muinck Keizer-Schrama S, Hogervorst E, Janse F, Liao L, Vlaisavljevic V, Zillikens C, Vermeulen N. ESHRE Guideline: management of women with premature ovarian insufficiency. Hum Reprod 2016; 31:926-937.

[ii] 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.

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. 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 NSD_GRP_OG_05-Endocrine-and-fertility-preservation-guidance-2022-v0.8.pdf (scot.nhs.uk).

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).
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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

[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.