Prescribing Guidelines

Trans woman medication
(This applies to a person assigned male, cis male, at birth undertaking gender transition to become a female)

These guidelines are to support GPs in the ongoing management of adult patients requiring life-long medication.

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1. Transfer of Prescribing Responsibilities from Secondary to Primary Care

In April 2016 NHS England Specialist Services Circular SSC1620 was issued which described Primary Care responsibilities in relation to prescribing and monitoring of hormone therapy for patients undergoing or having undergone Gender Dysphoria treatments. NHSE commission gender dysphoria services, the service specification includes current prescribing arrangements for hormone treatment, that being the prescribing and monitoring is undertaken in primary care, on the recommendation of a registered medical practitioner in the MDT of the specialist gender identity clinic. The General Medical Council (GMC) have information to support the care and treatment of *Transgender Patients*. It includes;

- Information on how to make your practice more inclusive
- Confidentially and equality consideration
- Prescribing responsibilities
- Mental Health and bridging prescriptions

The Specialist Gender Identity service will assist primary care by providing specific, relevant information and support for prescribing and monitoring, including the interpretation of blood test results. During and after a patient has completed the care pathway and has been discharged by the Specialist service, GPs should offer them the usual range of primary healthcare services that are available to other patients.

This guideline applies to patients who are of an age of majority to be able to provide informed consent i.e. over the age of 18

Special circumstances.

There has been an increase in the number of patients seeking bridging prescriptions prior to any formal diagnosis or who are accessing treatment from private Gender Identity Clinics, with accompanying requests for their GP to prescribe. For information on dealing with such requests see Appendix 2.

The Gender Identity Clinic staff at Porterbrook can give general advice and guidance in these circumstances. Such advice and guidance might relate to factors to consider in assessment and potential strategies but it will not be specific to a particular patient or constitute a recommendation.

2. Roles and responsibilities

Responsibilities of the primary care clinician

- To refer appropriate patients to Gender Identity Clinics for assessment. (see appendix 3 if patients may benefit from support whilst waiting to be seen)
- To agree to prescribe for patients in line with the prescribing guidelines
- To continue to prescribe for the patient as advised by the consultant
- To undertake monitoring as per prescribing guidelines (see table).

- As requested by the patient/clinic, refer the patients that are not invited by the national programme for breast or AAA screening (see section 10). If a patient changes their registered sex at the practice, discuss how this has implications for them with regard to national screening programmes.
- To adjust estradiol doses to maintain serum levels within the target range (Appendix 1)
- To seek the advice of the consultant if there are any concerns with the patient's therapy, please ensure all relevant blood monitoring has been performed and is included in the communication. Note, if seeking advice from the specialist specifically around blood monitoring results, communication should include; latest test results and a covering letter to capture the specific question / concern.

Responsibilities of consultant clinician

- To assess patients in line with the NHSE service specification.
- To liaise with referring GP if concerns with baseline monitoring
- To discuss benefits and side effects of treatment with the patient/carer and obtain written consent. This is particularly important for unlicensed products and when prescribing products outside of their licensed indications. A copy of the consent should be shared with the individual and the patients GP.
- To consider and discuss with the patient their individual requirements for national screening programmes (see section 10). The patients registered sex and the hormone treatment being taking can affect both the need for screening and whether the national screening programmes invite patients for screening. Risks and mitigating actions should be discussed and agreed with the patient and shared with primary care.
- To provide the details of the medication recommended, and the patients agreed personal goals, targets and a copy\link to the prescribing guidelines.
- To contact patient's GP to request prescribing is commenced and continued and send a link to, or a copy of the prescribing guidelines.
- Timely discuss any concerns with the GP regarding the patient's therapy
- To provide the GP with clear instructions including duration of treatment, details of monitoring and screening and re-referral criteria following the patients discharge from the specialist service.

3. Medication

All the medication in these guidelines are unlicensed for the indications for which they are being used.

Hormone treatment

The choice of hormone preparation, formulation and dosage is in line with current understanding of minimum health risks and maximum efficacy. Where an individual has a medical condition that may impact on hormone treatment or vice versa, the specialist clinician may request that the GP refers the patient to the endocrinology service.

Drug	Route/ Formulation	Dose	Comments
Estradiol	Oral/tablets	1-10mg daily	
	Transdermal/gel; 0.06% pump gel (delivers 0.75mg per actuation - Oestrogel®) or 0.5mg or 1mg sachets (Sandrena®)	2-6 measures daily (1.5mg-4.5mg) Or 0.5mg to 1.5mg daily, maximum dose 3mg	Particularly in patients over 40 years, *smokers or those with liver disease due to lower risk of thrombosis and liver dysfunction.
	Transdermal / patches	50 - 200 micrograms twice /week	
Dosage of estradiol therapy depends on circulating serum estradiol levels and clinical effects. The dose will be gradually increased to achieve a maximum degree of feminisation. This is particularly relevant for breast development. Patients should be advised to examine breasts every 3 months in the first year to ensure normal breast development, they should be encouraged to report any changes such as lumps, asymmetry and breast disfigurement. • Estradiol levels should be in the upper half- third of the normal follicular range (350--750 pmol/L); in older patients (>50 years) aim >200pmol/l at lower end of normal range. • Prolactin should be less than 1000mU/L – refer to local endocrinologist if above this level. If baseline level above 400mU/L Porterbook will consider need for cannulated prolactin to rule out stress induced;			

* There is strong evidence that an individual's risk of thrombosis is increased if they smoke, particularly if they are treated with estradiol. Consensus opinion amongst specialist medical practitioners is that individuals who smoke should desist whilst using hormone therapies, and particularly if they are treated with estradiol. Whilst smoking is not an exclusion to access to this treatment, hormone therapy should only be recommended following an individualised discussion of risk, possible adverse effects and possible impacts on final treatment outcome. Transdermal formulations are preferred.

GnRH Analogue

Drug	Route/ Formulation	Dose	Comments
Leuprorelin	sub-cutaneous injection	Initially two injections of 3.75mg (=7.5mg total dose) every month. If tolerated, change to 11.25mg every 3 months	The goal is for patients to self-administer. Practices may have to administer the initial injections and teach patients how to self-administer; side effects include liver dysfunction, diabetes

GnRH analogues are stopped post gonadectomy

- GnRH analogues are usually required to achieve maximum suppression of the secondary male sexual characteristics.
- They are introduced after or alongside estradiol
- Treatment goal is to achieve equivalent female levels of testosterone.
- Allows patients electing for gonadectomy to experience a post-surgical hormonal milieu.
- Inhibit the secretion of pituitary gonadotrophins leading to low circulating levels of testosterone

Adjunctive anti-androgen treatments if clinically indicated

These are effective, well tolerated and generally not associated with significant side effects

- Many listed side effects i.e. feminising effects such as gynecomastia and erectile dysfunction, are treatment goals in trans women
- Co-administration of estradiol avoids hypogonadism and reduces risk of other side effects, such as hot flushes, depression and osteoporosis

Drug	Route/ Formulation	Dose	Comments
Finasteride Reports of depression and, in rare cases, suicidal thoughts in men taking finasteride 1 mg (Propecia) for male pattern hair loss. Be aware that depression is also associated with finasteride 5 mg (Proscar). (MHRA May 2017). May cause metabolic complications	Oral/tablets	5mg daily	Blocks conversion of testosterone to dihydrotestosterone. Discourages male pattern hair loss and testosterone dependent body hair growth. Recommended for a time limited period only, prior to introduction of GnRH analogues to reduce male pattern hair loss. Can be used instead of GnRH analogues if patient prefers oral medication.

Cyproterone	Oral/tablets	50-100mg daily	Recommended for a brief period, on initiation of GnRH analogues to prevent a testosterone surge. May cause depression, liver disorders, meningiomas, adrenal suppression
Spironolactone	Oral/tablets	100-200mg daily	Occasionally used. Causes hyperkalaemia + hyponatraemia. Long-term use associated with liver dysfunction + possible hepatoma risk. May inhibit breast development and therefore should not be started until breast development is adequate (Tanner stage 3 / 4)
• Cyproterone and spironolactone are not recommended for long-term therapy due to their adverse effects profile • The gender identity clinic will provide the GP with information on course length and will review.			

Transition to Non-binary gender identity

Some birth assigned males have gender dysphoria but do not wish to fully transition to a female gender role and may wish to express a non-binary gender identity. If this is the objective, a more bespoke approach may be required and the GIC will provide detailed prescribing advice. The monitoring requirements are likely to be the same, but serum estradiol target ranges may be different.

4. Monitoring Requirements

- **In the first year every 3 months then every 6 months for the following 2 years after starting therapy**
- **Yearly thereafter**

Test/Measurement	**Recommended action if results outside of the normal range**	**Comments**
Body Mass Index	Offer to refer to local weight loss services if BMI is over 30. BMI under 40 is desired (but not essential) prior to commencing hormone therapy.	Only necessary if the patient is considering surgery. Surgery may be declined if BMI over 30. Risk / benefits of treatment to be considered by specialist
Blood Pressure	Treat in accordance with local hypertension guidelines if BP greater than 140/90mmHg	All patients
Urea and electrolytes	Check renal function and serum potassium.	Especially if the patient is taking spironolactone
Liver function tests	Refer to gastroenterology for advice if LFTs more than 3 times the upper normal limit.	All patients at risk of elevated LFTs
HbA1c	Treat in accordance with local diabetes guidelines	All patients have an increased diabetes risk with hormonal treatment
Lipid Profile	Treat in accordance with local lipid management guidelines	Increased CVS risk with hormonal therapy
TSH 0.27 – 4.2miu\l	Refer to endocrinology if outside the normal range or treat in accordance with local guidelines	
Fasting Serum morning testosterone <1.8nmol/l	Seek advice from Porterbrook or the patients original gender identity clinic if above 1.8nmol/l and measure LH/FSH	
Serum estradiol 350-750 pmol\L *(*see below for information on when to take blood samples)*	Titrate estradiol doses until the serum levels are within the therapeutic range. (See appendix 1)	Seek advice from Porterbrook or the patient's original gender identity clinic if unable to achieve appropriate serum levels within the estradiol dosage range.
Serum prolactin < 1000mU/L Baseline result <400mU/L	If above 1000mU/L on follow up refer to local endocrinologist. Note, If baseline level above 400mU/L Porterbook will consider need for cannulated prolactin to rule out stress induced hyperprolactinaemia and look for other cause	Refer to local endocrinologist to assess for a possible cause
Also see section 10 on page 11 for National screening advice		

* For patients taking Estradiol, blood tests should be performed:
    - 24 hrs after taking a tablet
    - 48 hours after a patch has been applied (Do not remove the patch)
    - 4-6 hours after the application of a gel

Risk and adverse effects of feminising hormones

Risk Level	Condition
Likely increased risk	Venous thromboembolic disease* Gallstones Elevated liver enzymes Weight gain Hypertriglyceridemia
Likely increased risk with presence of additional CVS risk factors (including age)	Cardiovascular disease** - encourage treatment of CV risk factors
Possible increased risk with presence of additional risk factors (including age)	Type 2 diabetes*
No increased risk or inconclusive	Breast Cancer

*Risk is greater with oral estradiol than with transdermal preparations

** Ideally use transdermal formulations in older patients

5. Hormone therapies and associated adverse effects

Adverse Effect	Comments
Thromboembolic disease	The incidence of deep venous thrombosis (DVT) in trans women is raised at approximately 2.6%. The majority occur during the first 2 years of treatment. An ongoing risk of 0.4% per year continues. If a thrombotic episode occurs, refer to specialist (heamatology/endocrinology) so a joint decision can be made. Treatment can be temporarily stopped until decisions are taken.
Breast cancer	The incidence of breast cancer with standard HRT in genetic females is increased. The risk of breast cancer secondary to feminising hormone therapy is likely to be low. Finasteride has been implicated in causing male breast cancer Trans woman Registered with a GP as a female A trans woman aged 50 to 70 who is registered with a GP as female, will be routinely invited for screening. Long-term hormone therapy can increase the risk of developing breast cancer so it is important that breast screening is considered usually at least after 5 years of feminising hormones and after age 50. Screening mammography every 3 years recommended. Making patient aware of breast cancer risk is important.

	Registered with a GP as male A trans woman aged 50 to 70 who is registered with a GP as male, will not be invited for breast screening. Long-term hormone therapy may increase the risk of developing breast cancer and breast screening should be considered
Hyperprolactinaemia	Estradiol therapy can result in hyperprolactinaemia and pituitary hypertrophy. The incidence of significant hyperprolactinaemia reported could be up to 15%
Prostate cancer	The incidence of prostate cancer is thought to be reduced in trans women compared with the cis male population. The prostate remains intact post-surgery.
Fertility	Estradiol therapy leads to a suppression of gonadotrophin production and subsequent reduction in spermatogenesis. Service users are counselled that treatment will reduce or remove their fertility, and gamete storage is discussed.
Abnormal liver function	Abnormalities of liver function are, rarely, associated with the use of estradiol therapy. The risk of abnormal liver function tests is approximately 3% in trans women. In half of these, the abnormalities persist for more than 3 months. However, the increases are mild and only rarely require discontinuation of treatment.
Age and mortality	When the patient reaches 40 years old consider transdermal estradiol preparations. Prolonged HRT use beyond 5 years after the menopause is associated with an increased risk of breast cancer in cis-females. Estradiol use beyond 55 years old in trans women appears safe from the point of view of breast health. Lifelong treatment is considered safe, in the absence of serious but rare conditions, although breast screening should continue beyond the age of 70, if estradiol is continued.

6. Treatment Outcomes

The effects of feminising hormones and the time to realise the desired outcomes are shown below.

Effect	**Expected onset**	**Expected maximum effect**
Body fat redistribution	3-6 months	2-5 years
Decreased muscle mass/ strength	3-6 months	1-2 years
Softening of skin/decreased oiliness	3-6 months	Unknown
Decreased libido	1-3 months	1-2 years
Decreased spontaneous	1-3 months	3-6 months

erections		
Male sexual dysfunction	Variable	Variable
Breast growth	3-6 months	2-3 years
Decreased testicular volume	3-6 months	2-3 years
Thinning and slowed growth of body and facial hair	6-12 months	
Decreased sperm production	Variable	Variable
Male pattern baldness	Loss stops 1-3 months, no growth	1 – 2 years

Note: This is a general guide and the timing of introduction of GnRH analogues may influence timescales

7. Managing treatments pre and post planned surgery

Due to an increased risk of venous thromboembolism, it is recommended that:

- Estradiol is stopped around 4-6 weeks before surgery resulting in immobility (including genital reconstructive surgery).
- GnRH analogues do not need to be stopped.
- Estradiol can be resumed 4 weeks post-operatively if there are no complications.
- After gonadectomy GnRH analogues are no longer required. However, rarely androgens may still be significantly derived from adrenal glands. If so finasteride can be prescribed.

8. Follow up and Discharge Arrangements

When service users are discharged from the service, detailed information is sent to the GP and service user. Guidance includes:

- Breast screening
- Prostate care advice (prostatectomy is not part of genital reconstructive surgery)
- Monitoring of bone health in individuals who have had a significant break from sex steroid treatment (>6 months).
- Ongoing treatment - estradiol is usually life long, in the absence of serious complications, although lower doses and circulating levels are acceptable in older trans women
- Long term goals and monitoring of hormone treatment, including target ranges for hormone levels
- Monitoring tests are needed for life 3 monthly for first year then 6 monthly for 2 years, then yearly thereafter if the patient remains well

- Action to take in response to common disorders and serious complications, including cessation of treatment
- When and where to seek specialist advice
- How to refer back or contact the Sheffield Gender Identity Clinic.

9. Screening

Which screening is necessary in Trans-woman.

See link for patient information leaflet, or NHS screening webpage more details on screening programmes for trans and non-binary people

Trans Woman	**What screening can be had?**	**Considerations** (See link (PIL) / link (web version) for patient information on screening programmes for trans and non-binary people)
Breast Screening	√	All patients **registered as a female** will be invited in for screening as per national screening programme. Patients **registered as male** will not be called up for screening. Long term hormones may increase risk of breast cancer. If, after discussion with the patient, screening is agreed, the GPs will need to refer to a local breast screening unit for a mammogram. Note the NHS Breast Screening Programme team are currently discussing ways to make the screening pathway more robust for all clients and in particular, the trans population.
Cervical Screening	×	All patients registered as a female will get invited in for cervical screening, this will not be required as trans women do not have a cervix. GPs can contact the national screening programme to request removal from the cervical screening invitation list
Abdominal aortic aneurysm screening	√	All patients **registered as a female** will not be invited in for screening Trans women have the same risk as a man and should consider accessing screening when they reach their 64th birthday. Patients can contact clinics directly or be referred in to arrange an appointment. See link to find local clinic details. Patients **registered as male** will be invited in for screening as per national screening programme.
Bowel screening	√	

It is not necessary to screen any more frequently that you would for a cis-woman.

Although there is no national screening for prostate cancer, PSA should be done after a prostate cancer risk assessment for those age 50 years or over, ongoing monitoring and management as per cis male.

10. For advice on on-going management contact

Porterbrook Clinic, Michael Carlisle Centre, 75 Osborne Road, Sheffield, S11 9BF, 01142716671

GP hormone advice line – 07811041506 (This line is exclusively for medical professionals who require **urgent** advice on hormone treatment and monitoring for transgender patients, call backs should be received within 48 hours, for non-urgent queries please write).

If the patient has been discharged and advice is needed around endocrine issues, then advice can be sought/patient referred to STH/local endocrine service

Also see website for information to support GPs - https://www.shsc.nhs.uk/services/gender-identity-clinic (scroll down page and click on 'information for GPs')

Training/education

Porterbrook run regular training and consultation workshops for general practitioners and primary care staff. If you are interested in attending a training session, please contact the clinic by emailing porterbrook@shsc.nhs.uk or calling 0114 2716671.

For external training around transhealth see;

- Royal College of GPs – Gender Variance training
- Centre of Pharmacy Postgraduate Education – Transgender Health, consulting with dignity and respect.
- Gender Identity Research and Education Society (GIRES) offer a number of courses to support care for transgender patients – See link

11. Bibliography

The role of the GP in caring for gender-questioning and transgender patients https://www.rcgp.org.uk/-/media/Files/Policy/A-Z-policy/2019/RCGP-position-statement-providing-care-for-gender-transgender-patients-june-2019.ashx?la=en

NHS England Specialised Services Circular 1826. Primary Care Responsibilities In Regard To Requests by Private On-Line Medical Service Providers to Prescribe Hormone Treatments for Transgender People. Available at: https://www.shsc.nhs.uk/sites/default/files/2021-03/Primary%20Care%20Responsibilities%20in%20regard%20to%20requests%20by%20Private%20On-line%20Medical%20Service%20Providers%20to%20Prescribe%20Hormone%20Treatments.pdf

Information for trans people: NHS Screening Programmes https://www.gov.uk/government/publications/nhs-population-screening-information-for-transgender-people/nhs-population-screening-information-for-trans-people

Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline The Journal of Clinical Endocrinology & Metabolism, Volume 102, Issue 11, 1 November 2017, Pages 3869–3903,

https://doi.org/10.1210/jc.2017-01658
Endocrinology of Transgender Medicine Endocrine Reviews, Volume 40, Issue 1, February 2019, Pages 97–117

Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People https://transcare.ucsf.edu/guidelines

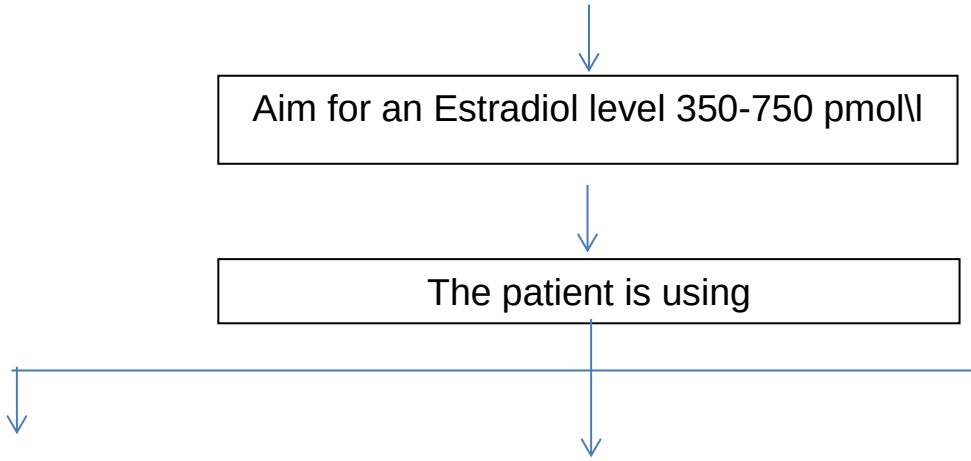
Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, Volume 102, Issue 11, 1 November 2017, Pages 3869–3903', is 100-200pg/ml (367-734pmol/L)

Identification of an optimal prolactin threshold to determine prolactinoma size using receiver operating characteristic analysis - https://www.nature.com/articles/s41598-021-89256-7.pdf

Pituitary Incidentaloma: An Endocrine Society Clinical Practice Guideline J Clin Endocrinol Metab. April 1, 2011; 96(4): 894–904. doi: 10.1210/jc.2010-1048

Appendix 1

Titration of **Estradiol**



For “menopausal” transwoman age 50-55 and above, serum estradiol levels at the lower end of the range and >200pmol/l are preferable. Transdermal formulations preferable in >40 year olds

	Oral Therapy	Gel	Patches
	Estradiol 1 – 10mg daily	0.5-4.5mg Estradiol daily	50-200 micrograms twice a week
Levels too low	Starting dose usually 1mg/day for first 6 months. Increase dose by 1mg /day then retest in 3 months – repeat until levels are in the desired range.	Pump dispenser (®Oestrogel) - The usual starting dose is two measures daily which contains 1.5mg estradiol for first 6 months. If required increase daily dose by one measure to achieve target levels and re-test in 3 months. (maximum 4.5mg/day) Sachets (®Sandrena Gel) - start with 0.5mg/day for first 6 months; Increase daily dose by 0.5mg every 3 months, if needed to achieve target levels (maximum 3mg/day)	Starting dose usually 50micrograms twice weekly for first 6 months. Increase twice weekly dose by 50 micrograms. Retest in 3 months and repeat until levels are in the desired range
Levels too high	Decrease dose by 1mg/day and retest in 3 months repeat until levels are in the desired range.	Decrease by 1 measure or 1 sachet daily. Retest in 3 months	Decrease twice weekly dose by 50 micrograms. Retest in 3 months until levels are in the desired range.

Appendix 2

For supporting information on ethical decisions regarding requests to prescribe hormone treatment to patients not under one of the NHSE commissioned services, see the following supporting documents.

- NHS specialised circular SSC1826 :Primary Care Responsibilities In Regard To Requests by Private On-Line Medical Service Providers to Prescribe Hormone Treatments for Transgender People

- GMC ethical hub – Mental Health and Bridging Prescriptions (note see 4th tab for information on 'mental health and bridging prescriptions'

Appendix 3 - Patient information

Gendered Intelligence is a free trans-led, confidential help and support service for patients waiting for their first appointment with a Gender Identify Clinic. The Gendered Intelligence can offer independent support and a listening ear at what we know can be a really difficult time for patients waiting.

The trans affirmative support they offer is provided by workers who are all trans and non-binary people themselves and have lived experience of gender identity services.

They can support patients to:

- access confidential support
- source helpful information
- chat about resilience and self-care
- talk about how you might handle difficult times
- take care of your wellbeing

Patients can contact them on Mondays, Tuesdays and Thursdays from 2pm to 7pm and Wednesdays and Fridays from 10am to 3pm.

Any contact outside of these hours will be picked up and responded to as soon as possible.

Patients can get in touch in whatever way they feel most comfortable:

- Telephone: 0330 3559 678
- Text message or WhatsApp: 07592 650 496
- Email: supportline@genderedintelligence.co.uk

To find out more about the support on offer visit genderedintelligence.co.uk

Patients can also contact one of our **Peer Support Workers** who have lived experience of using gender identity services and they can support, offer guidance, or answer any questions the patient may have about what to expect from the service. They can be contacted by emailing porterbrooksupport@shsc.nhs.uk.