Doncaster & Bassetlaw Area Prescribing Committee has approved this guidance for use by Prescribers in Primary Care that choose to prescribe. This is not a mandatory document

Barnsley, Rotherham & Sheffield
Clinical Commissioning Groups

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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 patients requiring life-long medication.

Prescribing Guidelines developed by:

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1. Transfer of Prescribing Responsibilities from Secondary to Primary Care

In March 2014 NHS England Specialist Services Circular SSC1417 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. In March 2016 the General Medical Council (GMC) published *Guidance for Doctors Treating Transgender Patients.* This guidance reiterates the advice previously set out by NHS England in SSC 1417; and explains the legal protection against discrimination and harassment given to trans people by the Equality Act 2010 and Gender Recognition Act 2004.

Those responsibilities include

- Prescribing hormone therapy,
- Patient safety monitoring,
- Provision of physical health examinations and blood tests under the guidance of a specialist Gender Identity service.

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.

2. Roles and responsibilities

Responsibilities of the primary care clinician:

- To refer appropriate patients to Gender Identity Clinics for assessment
- 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.
- 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.

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Responsibilities of consultant clinician

- To discuss benefits and side effects of treatment with the patient/carer and obtain informed consent. This is particularly important for unlicensed products and when prescribing products outside of their licensed indications.
- 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.
- To discuss any concerns with the GP regarding the patient's therapy
- To provide the GP with clear instructions including referral criteria following the patients discharge from the specialist service

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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	1-6mg daily	
	0.06% gel	2-4 measures daily (1.5mg-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.

- Estradiol levels should be in the upper half-third of the normal follicular range (300-600 pmol/L)
- Prolactin should be less than 400 mU/L.

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 increase 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

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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)	oral	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	50-100mg daily	Recommended for a brief period, on initiation of GnRH analogues to prevent a testosterone surge.
Spironolactone	oral	100-200mg daily	Occasionally used. Causes hyperkalaemia + hyponatraemia. Long-term use associated with liver dysfunction + possible hepatoma risk. May inhibit breast development.
• 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.			

4. Monitoring Requirements

- **Every 6 months for 3 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.	Only necessary if the patient is considering surgery. Surgery may be declined if BMI over 30.
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 LFT's more than 3 times the upper normal limit.	All patients at risk of elevated LFT's
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 0.38-5.5 miu\l	Refer to endocrinology if outside the normal range	
Serum testosterone <1.8nmol/l	Seek advice from Porterbrook or the patients original gender identity clinic if above 1.8nmol/l	
Serum estradiol 300-600 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 < 400mU/L	Seek advice from Porterbrook or the patients original gender identity clinic if above 400mU/L	Consider cannulated prolactin to rule out stress induced prolactinaemia

*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

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5. 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
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

6. 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.
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 *Registered with a GP as male* A 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 be should consider
Hyperprolactinaemia	Estradiol therapy can result in hyperprolactinaemia and pituitary hypertrophy. The incidence of significant hyperprolactinaemia reported could to be up to 15%

Adverse Effects	Comments
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.

7. 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 erections	1-3 months	3-6 months
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

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8. 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.

9. 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
- Prostrate screening (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 on 6 monthly basis for 3 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.

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10. Screening

Which screening is necessary Trans-woman.

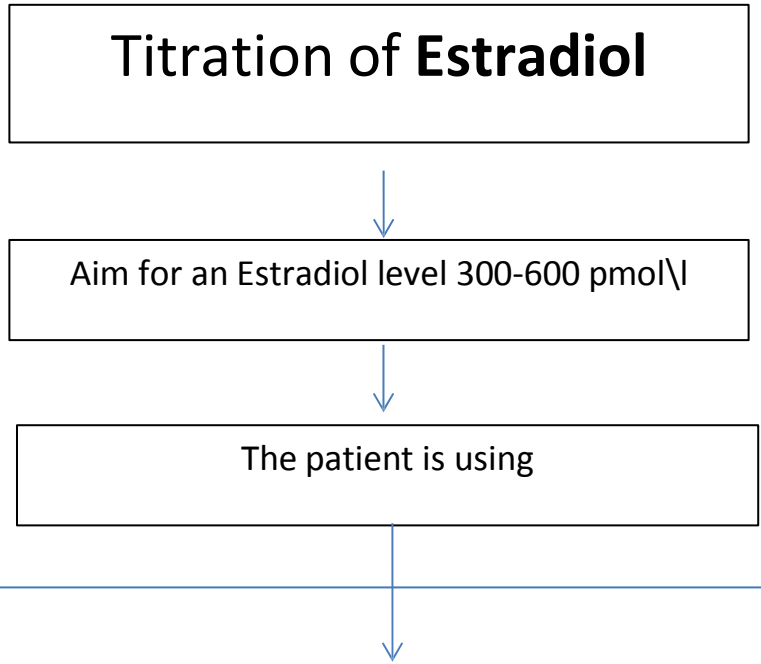
Trans Woman	
Breast Screening	√
Cervical Screening	×
Abdominal aortic aneurysm screening	√
Bowel screening	√

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

11. For advice on on-going management contact;

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

Appendix 1



For "menopausal transwoman age 50-55 and above serum estradiol levels at the lower end of the range are preferable.

	Oral Therapy	Gel	Patches
	Estradiol 1 – 6mg daily	1 – 4 measures = 0.75-3mg Estradiol	50-200 micrograms twice a week
Levels too low	Increase dose by 1mg retest in 3 months – repeat until levels are in the desired range.	The usual starting dose is two measures which contains 1.5mg estradiol. Increase dose by one measure and re-test in 3 months.	Increase dose by 50 micrograms. retest in 3 months and repeat until levels are in the desired range
Levels too high	Decrease dose by 1mg and retest in 3 months repeat until levels are in the desired range.	Decrease by 1 measure. Re test in 3 months	Decrease dose by 50 micrograms retest in 3 months until levels are in the desired range.