

## Hormone Therapy in Gender Dysphoria

Prescribing for **trans women** (this applies to a person assigned male, cis-male, at birth undertaking gender transition to become a female)

## **Prescribing Information Sheet:** To be read in conjunction with the relevant SPCs

NHS England (NHSE) commission specialist gender identity centres. NHSE have stated that the patient's GP is responsible for organising blood and other diagnostic tests and for prescribing pharmacological treatments as recommended by the specialist identity centres. The Specialist Gender Identity service will assist by providing relevant information and support for prescribing and monitoring, including the interpretation of blood test results. It is therefore likely that GPs will be requested to prescribe hormones for patients that are under the care of a specialist identity centre.

# However, NHSE has also stated that NHS GICs should retain responsibility for providing prescriptions and for monitoring until the GP has agreed to a transfer of responsibilities. Individual prescribers MUST only prescribe within their own level of competence.

The local gender identity centre is in Leeds which forms part of the Leeds and York Partnership NHS Foundation Trust.

The General Medical Council (GMC) have put together a set of ethical guidance on trans healthcare which can be accessed via: <a href="https://www.gmc-uk.org/ethical-guidance/ethical-hub/trans-healthcare">https://www.gmc-uk.org/ethical-guidance/ethical-hub/trans-healthcare</a>.

## IMPORTANT INFORMATION

## NHS England has stated the following concerning gender incongruence and/or gender dysphoria for those < 18 years:

Patients under 18 years of age **must not** be prescribed puberty-suppressing hormones. This includes both private and NHS treatment.

## Additionally:

GPs **must** refuse to support the private prescribing or supply of GnRH analogues.

GPs **should** refuse to support an unregulated provider in the prescribing or supply of alternative medications that may be used to suppress pubertal development.

GPs **should** refuse to support an unregulated provider in the prescribing of exogenous hormones.

### Prescribing for those 18 or over:

GPs should evaluate requests for shared care by confirming that the request originates from a reputable provider and an appropriate gender specialist. GPs may decline to prescribe if safety concerns arise, as long as this does not create a significant clinical risk to the patient.

**Please note:** The Medicines (Gonadotrophin-Releasing Hormone Analogues) (Restrictions on Private Sales and Supplies) (England, Wales and Scotland) Order 2024 imposes a prohibition on the sale or supply of certain medicinal products that contain gonadotrophin-releasing hormone analogues (GnRH analogues): This means that GnRH analogues cannot be prescribed to **private patients** under 18 for gender dysphoria/gender incongruence unless commenced before 3rd June 2024. The Order applies to England, Wales, Northern Ireland and Scotland.

The following tables contain information relating to the most commonly requested hormone replacement therapies. This information relates to trans women (a person assigned male, cis-male, at birth undertaking gender transition to become a female) only. There is a separate prescribing sheet available for trans men (a person assigned female, cis-female, at birth undertaking gender transition to become a male) available on the LSCMMG website via <a href="https://www.lancashireandsouthcumbriaformulary.nhs.uk/">https://www.lancashireandsouthcumbriaformulary.nhs.uk/</a>.

Medication	Typical Dosing and Product Information off label use	Additional Information (See table 3 and 4 for Side Effects and Interactions)
stradiol PO Generic and proprietary – 1 to 10mg daily		The dose is gradually increased to achieve a maximum degree of feminisation.
Estradiol PC	Oestrogel® Pump-Pack 0.06% gel – TWO to SIX measures (1.5 to 4.5mg) daily or Sandrena sachets 0.5mg to 1.5mg daily, maximum dose 3mg Transdermal patch e.g. Evorel® - 50 to 200microgram TWICE weekly	Transdermal preparations should be offered to patients over 40 years, smokers or those with liver disease as they have been associated with a lowe risk of thrombosis and liver dysfunction
GnRH analogues and anti-androgen However, rarely androgens may still be significant	<b>treatment. Please note:</b> the following gonadectomy Gnl ntly derived from adrenal glands. If so, an anti-androgen may	RH analogues are no longer required. / still be indicated.
Leuprorelin acetate SC	Prostap® SR DCS or Prostap® 3 DCS – initially 7.5mg every month increased to 11.25mg every THREE months (as advised by the specialist centre).	Can be considered for self - administration. Introduced alongside estradiol. Aim to achieve equivalent female levels of testosterone.
Triptorelin embonate IM	Decapeptyl SR 22.5mg IM every SIX months (as advised by the specialist centre) – <b>see additional</b> <b>information</b>	To be considered for those that are tolerating GnRH analogues but timely administration of a shorter acting analogue is not possible.
Finasteride PO Prescribers must be aware that patients should be advised to stop finasteride immediately and inform a healthcare professional if they develop depression – <u>MHRA/CHM advice May 2017</u>	Generic – 5mg daily	Adjunctive anti-androgen treatment (if clinically indicated). 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 the patient prefers oral medication.
Spironolactone PO	Generic – 100 to 200mg daily	Adjunctive anti-androgen treatment (if clinically indicated). Not recommended for long-term use due to adverse effect profile.

 Table 2. Suggested dose adjustment of estradiol therapy.
 Seek advice from the patient's original gender identity clinic if unable to achieve levels in the therapeutic range.

**Dose titration of estradiol oral preparations:** if the estradiol level (taken 24hours after the last oral dose) is <350pmol/L increase the dose by 1mg. If the estradiol level is >750pmol/L decrease the dose by 1mg. In both cases recheck levels in 12-weeks.

Dose titration of estradiol gel preparations: Oestrogel® Pump-Pack 0.06% gel/Sandrena® Gel: if the estradiol level (taken 4 – 6 hours after application) is <350pmol/L increase the dose by ONE measure (0.75mg) or 0.5mg of Sandrena® Gel. If the estradiol level is >750pmol/L decrease the dose by ONE measure (0.75mg) or O.5mg backet (0.5mg) daily. In both cases recheck levels in 12-weeks.

**Dose titration of estradiol patches:** if the estradiol level (taken 48hours after patch application – do not remove the patch) is <350pmol/L increase the dose by 50micrograms (to be administered TWICE weekly). If the estradiol level is >750pmol/L decrease the dose by 50microgram (to be administered TWICE weekly). In both cases recheck levels after 12-weeks.

## Table 3. Monitoring and review requirements

The following tests or measurements should be monitored in primary care every THREE months in the first year, then every SIX months for THREE years after starting hormone therapy, and continued ONCE yearly thereafter.

Test or Measurement	Recommended action if the result is outside of the normal range	
Body Mass Index	Manage according to local guidelines if BMI increases to over 30 – only necessary in this context if the patient is considering surgery. BMI under 40 is desired (but not essential) prior to commencing hormone therapy.	
Blood pressure	Manage according to local guidelines if BP greater than 140/90mmHg.	
Urea and electrolytes	If out-of-range, seek further advice from the patient's original gender identity clinic.	
Liver function tests	nction tests If elevated, refer to gastroenterology – seek further advice from the patient's original gen identity clinic.	
HbA1c	If elevated, manage according to local guidelines.	
Lipid profile	If elevated, manage according to local guidelines.	
TSH	If elevated, refer to endocrinology.	
Fasting serum morning testosterone		
Serum estradiol	Target range <b>350 to 750pmol/L</b> ; Seek advice from the patient's original gender identity clinic if unable to achieve level in the therapeutic range.	
Serum prolactin	I prolactin         If above 1000mU/L on follow up refer to local endocrinologist to assess possible cause           Target range < 400mU/L; Seek advice from the patient's original gender identity clinic	

Estradiol	
Likely increased risk	Common or very common
Venous thromboembolic disease Gallstones Elevated liver enzymes Weight gain Hypertriglyceridemia	Appetite decreased; arthralgia; bone pain; breast abnormalities; depression; dizziness; fatigue; gynaecomastia; headache hepatic disorders; hot flush; hyperhidrosis; injection site necrosis; insomnia; mood altered; muscle weakness; arthralgia; nausea; peripheral oedema; sexual dysfunction; testicular
Likely increased risk with presence of additional CVS risk factors (including age)	atrophy; vulvovaginal dryness; weight change
Cardiovascular disease	Alopecia; paraesthesia; dizziness; weakness of lower extremities; diarrhoea; fever; myalgia; palpitations; visual impairment; vomiting
Conditions which need supervision	

Table 4. Summary of medication side effects Please refer to the individual medications SPC for more details

Type 2 diabetes, risk factors for thromboembolic disorders, hypertension, liver disorders, migraine, lupus, epilepsy, asthma, Otosclerosis.

Low increased risk or inconclusive Breast Cancer

Cyproterone

#### Common or very common

Depressed mood; dyspnoea; fatigue; gynaecomastia; hepatic disorders; hot flush; hyperhidrosis; restlessness; weight change **Uncommon** 

Skin reactions

Rare or very rare

Galactorrhoea; neoplasms; hypersensitivity

#### Frequency not known

Adrenocortical suppression; anaemia; azoospermia; hair changes; hypotrichosis; osteoporosis; sebaceous gland underactivity (may clear acne); thromboembolism

#### PLEASE NOTE:

Direct hepatic toxicity including jaundice, hepatitis and hepatic failure have been reported with cyproterone (fatalities reported, usually after several months, at dosages of 100 mg and above). If hepatotoxicity is confirmed, cyproterone should normally be withdrawn unless the hepatotoxicity can be explained by another cause such as metastatic disease (in which case

### Rare or very rare

Haemorrhage

#### Frequency not known

Anaemia; glucose tolerance impaired; hypertension; hypotension; leucopenia; paralysis; pulmonary embolism; QT interval prolongation; seizure; spinal fracture; thrombocytopenia; urinary tract obstruction

#### **Finasteride**

#### Common or very common

Sexual dysfunction

#### Uncommon

Breast abnormalities; skin reactions

#### Frequency not known

Angioedema; depression; infertility male; palpitations; testicular pain

#### **Triptorelin**

#### Common or very common

Asthenia; depression; diabetes mellitus; dizziness; dry mouth; embolism; gastrointestinal discomfort; gynaecomastia; haemorrhage; headache; hot flush; hyperhidrosis; hypersensitivity; hypertension; joint disorders; menstrual cycle irregularities; mood altered; muscle complaints; nausea; oedema; ovarian and fallopian tube

cyproterone should be continued only if the perceived benefit	disorders; pain; painful sexual intercourse; pelvic pain;
exceeds the risk).	sexual dysfunction; skin reactions; sleep disorders; weight
Spironolactone	changes; injection site reaction
Common or Very Common	
	Uncommon
Hyperkalaemia; confusional state; dizziness; nausea; pruritis;	
rash; muscle spasms; acute kidney injury; gynaecomastia;	Alopecia; appetite abnormal; asthma exacerbated; chills;
malaise	confusion; constipation; diarrhoea; drowsiness; dyspnoea;
	flatulence; gout; muscle weakness; taste altered; testicular
Uncommon	disorders; tinnitus; vertigo; vision disorders; vomiting;
	thrombocytosis; diabetes mellitus; hyperlipidaemia; insomnia;
Electrolyte imbalance; hepatic function abnormal; urticaria	paraesthesia; palpitations; epistaxis; abdominal pain; acne;
	rash (various types); pruritis; muscle disorders; bone pain;
Frequency not known	arthralgia; nocturia; urinary retention; gynaecomastia;
Acidosis hyperchloraemic, acute kidney	lethargy; peripheral oedema; pain; rigors; somnolence
injury; agranulocytosis; alopecia; breast neoplasm	
benign; breast pain; confusion; dizziness; electrolyte	Rare or very rare
imbalance; gastrointestinal disorder; gynaecomastia; hepatic	
function abnormal; hyperkalaemia	Abnormal sensation in eye; chest pain; difficulty standing;
(discontinue); hypertrichosis; leg cramps; leucopenia; libido	fever; hypotension; influenza like illness; musculoskeletal
disorder; malaise; menstrual disorder; nausea; severe	stiffness; nasopharyngitis; orthopnoea; osteoarthritis;
cutaneous adverse reactions (SCARs); skin	memory impairment; joint problems; pyrexia; dysstasia
reactions; thrombocytopenia	
	Frequency not known
	Angioedema; malaise; urinary incontinence QT interval
	prolongation; anxiety
<b>Table 5. Interactions</b> Please refer to the individual medications	s STC Tor more details

#### **Estradiol**

Medicines which either increase or decrease clearance of estradiol such as CYP450 enzymes inducers/inhibitors (see BNF/SPC).

#### Leuprorelin and triptorelin

No interactions listed in the BNF.

#### <u>Finasteride</u>

Although the risk for finasteride to affect the pharmacokinetics of other drugs is estimated to be small, it is probable that inhibitors and inducers of cytochrome P450 3A4 will affect the plasma concentration of finasteride.

#### Spironolactone

Spironolactone might oppose the effects of Abiraterone (interaction classed as severe by the BNF). Manufacturer advises avoid.

#### **Cyproterone**

Several CYP450 enzyme inducers may decrease the efficacy of cyproterone (See BNF for list of severe interactions).

#### Bibliography

- 1. General Medical Council (GMC). Trans healthcare 2019 [Available from: <u>https://www.gmc-uk.org/ethical-guidance/ethical-hub/trans-healthcare</u>] [Accessed online August 2024].
- 2. Royal Pharmaceutical Society. BNF: British National Formulary NICÉ. 2024. Accessed via <u>www.nice.bnf.org.uk</u> [accessed online: October 2024].
- NHS England policy: Prescribing of Gender Affirming Hormones (GAH; masculinising or feminising hormones) as part of the Children and Young People's Gender Service is available via <u>https://www.england.nhs.uk/wpcontent/uploads/2024/03/clinical-commissioning-policy-prescribing-of-gender-affirming-hormones.pdf</u> [Accessed online August 2024]
- 4. Sheffield Gender Idenity Clinic. Prescribing Guidelines: Trans woman medication (This applies to a person assigned male, cis-male, at birth undertaking gender transition to become a female). Sheffield Health and Social Care NHS Foundation Trust (updated July 2022).
- 5. <u>The Medicines (Gonadotrophin-Releasing Hormone Analogues) (Restrictions on Private Sales and Supplies) Order</u> 2024

Please access this guidance via the LSCMMG website to ensure that the correct version is in use.

_	Version Control		
	Version Number	Date	Amendments Made
	Version 1.0	July 2019	New guideline. AG

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Version 1.1	September 2019	When to stop GnRH analogues added. AG.
Version 1.2	March 2021	Prescribing responsibility updated. AG.
Version 1.3	July 2021	Triptorelin added. AG.
Version 1.4	December 2023	Amended to align with updated Sheffield Guidance and SPCs.
Version 1.5	September 2024	Amended to align with updated NHSE policy.
Version 1.6	December 2024	References updated to include Government legislation.
Version 1.7	May 2025	Information and guidance in relation to update to the PSH statutory instrument updated.

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