Hormone Therapy in Gender Dysphoria

AMBER0

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: https://www.gmc-uk.org/ethical-guidance/ethical-hub/trans-healthcare. A summary of the main points follows:

- GPs can prescribe unlicensed medicines following the steps set out in GMC guidance
- If a patient is self-medicating with hormones that have been purchased, consider issuing a bridging prescription as part of a harm reduction approach. Seek the advice of an experienced gender specialist.

IMPORTANT INFORMATION

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

NHS England has decided **not to commission puberty-suppressing hormones (PSH)** for children and young people with gender incongruence/gender dysphoria due to a lack of evidence on safety, effectiveness, and ethics.

NHS England has stated that the commissioning **of gender-affirming hormones (GAH) will be managed through the relevant local NHS England Specialised Commissioning Team**, and Integrated Care Boards will fund the costs of GAH for each patient.

The 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 https://www.england.nhs.uk/wp-content/uploads/2024/03/clinical-commissioning-policy-prescribing-of-gender-affirming-hormones.pdf The policy lists criteria that the young person must meet to receive GAH therapy also lists conditions that make the young person ineligible for GAH therapy.

Please note: In addition to the NHSE policy, The Medicines (Gonadotrophin-Releasing Hormone Analogues) (Emergency Prohibition) (England, Wales and Scotland) Order 2024 imposes an emergency 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 and was extended to November 2024.

NHS primary care prescribers receiving requests from private specialist prescribers to commence or continue GnRH analogues for patients under the age of 18 must be refused.

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 www.lancsmmg.nhs.uk.

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Table 1. Preparations for trans women adult patients (this applies to a person assigned male, cis-male, at birth undertaking gender transition to become a female)		
Medication	**Typical Dosing and Product Information** off label use	**Additional Information** (See table 3 and 4 for Side Effects and Interactions)
Estradiol 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 lower risk of thrombosis and liver dysfunction.
GnRH analogues and anti-androgen treatment. Please note: the following gonadectomy GnRH analogues are no longer required. However, rarely androgens may still be significantly derived from adrenal glands. If so, an anti-androgen may 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) – **see additional information**	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** – MHRA/CHM advice May 2017	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.
Cyproterone PO	Generic – 50 to 100mg daily	Recommended for a short period on initiation of GnRH analogues to prevent a testosterone surge.

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 ONE sachet (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 50microgams (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	If elevated, refer to gastroenterology – seek further advice from the patient's original gender 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	Target **<1.8nmol/L**; Seek advice from the patient's original gender identity clinic if elevated and measure LH/FSH.
Serum estradiol	Target range **350 to 750pmol/L**; Seek advice from the patient's original gender identity clinic if unable to achieve level in the therapeutic range.
Serum 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 if elevated >400mU/L but <1000mU/L.

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

Estradiol

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

Conditions which need supervision

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

Leuprorelin

Common or very common

Appetite decreased; arthralgia; bone pain; breast abnormalities; depression; dizziness; fatigue; gynaecomastia; headache; he patic disorders; hot flush; hyperhidrosis; injection site necrosis; insomnia; mood altered; muscle weakness; arthralgia; nausea; peripheral oedema; sexual dysfunction; testicular atrophy; vulvovaginal dryness; weight change

Uncommon
Alopecia; paraesthesia; dizziness; weakness of lower extremities; diarrhoea; fever; myalgia; palpitations; visual impairment; vomiting

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

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

Table 5. Interactions Please refer to the individual medications SPC for 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.

Finasteride

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: https://www.gmc-uk.org/ethical-guidance/ethical-hub/trans-healthcare] [Accessed online August 2024].
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3. 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 https://www.england.nhs.uk/wp-content/uploads/2024/03/clinical-commissioning-policy-prescribing-of-gender-affirming-hormones.pdf [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. The Medicines (Gonadotrophin-Releasing Hormone Analogues) (Restrictions on Private Sales and Supplies) Order 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

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.

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