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. Therefore, it is 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 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.

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 LMMG website via www.lancsmmg.nhs.uk.

Table 1. Preparations for trans women (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 6mg daily	The dose is gradually increased to achieve a maximum degree of feminisation.
Estradiol PC	Oestrogel® Pump-Pack 0.06% gel – TWO to FOUR measures (1.5 to 3mg) daily 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: 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.
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 <300pmol/L increase the dose by 1mg. If the estradiol level is >600pmol/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: if the estradiol level (taken 4 – 6 hours after application) is <300pmol/L increase the dose by ONE measure (0.75mg). If the estradiol level is >600pmol/L decrease the dose by ONE measure (0.75mg). 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 <300pmol/L increase the dose by 50microgams (to be administered TWICE weekly. If the estradiol level is >600pmol/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 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.
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.
Serum testosterone	Target **<1.8nmol/L**; Seek advice from the patient's original gender identity clinic if elevated.
Serum estradiol	Target range **300 to 600pmol/L**; Seek advice from the patient's original gender identity clinic if unable to achieve level in the therapeutic range.
Serum prolactin	Target range **< 400mU/L**; Seek advice from the patient's original gender identity clinic if elevated.

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

Possible increased risk with presence of additional risk factors (including age)

Type 2 diabetes*

No increased risk or inconclusive

Breast Cancer

Cyproterone

Common or very common

Depressed mood; dyspnoea; fatigue; gynaecomastia; hepatic disorders; hot flush; hyperhidrosis; nipple pain; restlessness; weight change

Uncommon

Skin reactions

Rare or very rare

Galactorrhoea; neoplasms

Leuprorelin

Common or very common

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; nausea; paraesthesia; peripheral oedema; sexual dysfunction; testicular atrophy; vulvovaginal dryness; weight change

Uncommon

Alopecia; 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 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 cyproterone should be continued only if the perceived benefit exceeds the risk).	**Frequency not known** Angioedema; depression; infertility male; palpitations; testicular pain **Spironolactone** **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

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

Estradiol

There is an increased (interaction classed as severe by the BNF) risk of venous thromboembolism (VTE) if hormone replacement therapy is given with the following: lenalidomide, pomalidomide and thalidomide.

Leuprorelin

The concomitant use of leuprorelin or triptorelin with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de pointes such as class IA (e.g. quinidine, disopyramide) or class III (e.g. amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, methadone, moxifloxacin, antipsychotics, etc. should be carefully evaluated.

Finasteride

St John's wort moderately reduces the exposure to finasteride; it is possible that finasteride may be less effective if co-administered with St John's wort.

Spironolactone

Spironolactone is predicted to decrease the effects of mitotane (interaction classed as severe by the BNF). Manufacturer advises avoid.

Cyproterone

No significant interactions listed in the BNF.

Bibliography

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5. The World Professional Association for Transgender Health (WPATH). Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People: The World Professional Association for Transgender Health; 2012. 112 p.
6. Takeda UK Ltd. Prostap 3 DCS - Summary of Product Characteristics (SmPC) - (eMC) of first authorisation: 28/04/2011Date of Renewal: 26/04/2016 [Available from: https://www.medicines.org.uk/emc/product/4651/smpc#.

Please access this guidance via the LMMG 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.

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