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# guidelines for gender-affirming primary care with trans and non-binary patients

## A QUICK REFERENCE GUIDE FOR PRIMARY CARE PROVIDERS (PCPs)

This quick reference guide was derived from Sherbourne's *Guidelines for Gender-Affirming Primary Care with Trans and Non-Binary Patients* and is designed to be used in conjunction with the full Guidelines.

**Key messages**

- Prescribing hormone therapy for trans patients is well-situated in primary care.
- The risks of witholding hormone therapy are often more substantial than the risks of treatment.

### AN INDIVIDUALIZED APPROACH

Given the spectrum of gender identity and the variation in each person's expression, there is no single pathway for a trans person to follow in order to actualize the presentation of their authentic self. Non-binary patients may also seek hormone therapy to modify their secondary sex characteristics.
When hormones are chosen as part of transition, some patients may seek maximum feminization/ masculinization, while others may seek a more androgynous appearance.

### DECISION TO INITIATE HORMONE THERAPY

The decision to initiate hormone therapy is a collaborative patient-centered process that focuses on both psychosocial preparation and informed consent. The PCP (with or without the support of a multi-disciplinary team) can facilitate a decision-making process that informs, educates and supports patients. For each patient seeking hormone therapy, it is important to not only consider the possible risks of treatment but to consider the often substantial risks of witholding treatment.

### TERMINOLOGY

**CIS:** Refers to a state of alignment of one's gender identity with the gender assigned at birth. You may also sometimes see "cissexual" or "cisgender." Thus, non-trans men are "cis men" and non-trans women are "cis women." It is preferable (and more accurate) to use "cis" than to use terms such as "bio", "genetic" or "real." It is also preferable to use "cis" rather than only using "woman" or "man" to describe non-trans persons. If cis is not used as a descriptor for non-trans persons, then such persons may be presumed to be the more "normal" or "valid" instantiation of that particular gender, thus contributing to cissexism.

**TRANS:** Umbrella term for people who are not cis, includes persons who are (or identify as) non-binary as well as transmasculine and transfeminine individuals.

**NON-BINARY:** Umbrella term for anyone who does not identify with static, binary gender identities. Includes persons who may identify as having an intermediary gender (e.g. genderqueer), as being multiple genders (e.g. bigender, polygender, etc.), as having a shifting gender (gender fluid), or as not having a gender altogether (agender).

**DISCLAIMER:**

*These guidelines reflect the current practice at Sherbourne Health in the management of trans patients. We do not present it as a 'Standard of Care' but instead as a guide to help clinicians in their day-to-day practice. Adaptions may be considered relating to each patient's unique circumstances. Clinicians must use their own expertise and decision-making skills within each clinical encounter.*

# Feminizing hormone therapy

**The goal of hormone therapy** in transfeminine patients is to reduce the endogenous effects of testosterone and to induce feminine secondary sex characteristics. Physiologically, this requires a suppression of endogenous androgens and the addition of estrogen. This treatment results in both reversible and irreversible feminization.[1]

## ANTI-ANDROGENS

The anti-androgens typically used at Sherbourne Health are spironolactone and cyproterone, with the former historically chosen preferentially as it was believed to have a superior safety profile. This practice has changed over time, as adequate anti-androgen effects and testosterone suppression into the female range are achievable at lower doses of cyproterone (i.e. 12.5 – 25mg daily) at which adverse effects are less likely.[2] Thus the choice of anti-androgen should be made individually for each patient based on their medical history and preference regarding risk and side effect profiles. Following orchiectomy (+/- vaginoplasty), most transfeminine patients will not require androgen suppression. The androgen-blocker can be stopped immediately after surgery or tapered over the course of 4-6 weeks or more depending on individual factors (e.g., patients with hypertension or renal dysfunction on spironolactone should be tapered).

## ESTROGENS

Estrogen acts directly on estrogen receptors to initiate feminization. Several forms and routes of estrogen have been used for feminization. At Sherbourne Health, the most common form used is oral 17-β estradiol (Estrace), which is covered by the ODB program. While conjugated estrogens (e.g. Premarin) have historically been used due to their accessibility/affordability, they are no longer recommended.[3] There is a lack of consensus on the preferred timing of the initiation of estrogens in relation to an anti-androgen. Common approaches have included both the initiation of an anti-androgen (usually 1-3 months) prior to the addition of estrogen, or alternatively, the simultaneous introduction and subsequent titration of both components. In patients over 50 years old who have been on estrogen for several years, doses may be reduced to those administered to post-menopausal cis women (e.g. starting/low dose topical formulations).

**Keep in mind:** In adolescent patients, the initiation of estrogen therapy prior to the completion of skeletal growth may lead to an earlier cessation of long bone growth and thus shorter adult height, an effect which would be irreversible. This may be a desired effect. Complete epiphyseal fusion can occur as early as age 14 and as late as age 19 in AMAB individuals.[4]

## PRECAUTIONS

Evidence compiled by the Endocrine Society suggests that feminizing hormone therapy is "**safe without a large risk of adverse events when followed carefully for a few well-documented medical concerns.**"[5]
Available measures to reduce risks associated with feminizing hormone therapy should be considered and discussed with patients and if possible, undertaken prior to or concurrently with hormone therapy.[6] Suggested measures to minimize risks associated with precautions may be found in the full Guidelines.

**Contraindications**

- Unstable ischemic cardiovascular disease
- Estrogen-dependent cancer
- End stage chronic liver disease
- Psychiatric conditions which limit the ability to provide informed consent
- Hypersensitivity to one of the components of the formulation

## FORMULATIONS AND RECOMMENDED DOSES OF ANTI-ANDROGENS AND ESTROGEN

| Formulations | Starting Dose | Usual Dose | Maximum Dose | Cost* (4 weeks) |
|---|---|---|---|---|
| Spironolactone (oral) | 50 mg daily - BID | 100 mg BID | 150 mg bid[a] | $15–$41 |
| Cyproterone (oral) | 12.5 mg (1/4 50 mg tab) q2d - daily | 12.5 mg (1/4 50 mg tab) – 25 mg (1/2 50 mg tab) daily | 50 mg daily[a] | $16–$56 |
| Estradiol (oral)* | 1–2mg daily | 4mg daily or 2mg bid | 6 mg daily or 3 mg BID | $18–$54 |
| Estradiol (transdermal, patch)*[b] | 50 mcg daily/apply patch 2x/ week | Variable[c] | 200 mcg daily/ apply patch 2x/ week | $39–$76[d] |
| Estradiol (transdermal, gel)*[e] | 2.5 g daily (2 pumps, contains 150 mcg estradiol) | Variable[c] | 6.25 g OD (5 pumps, contains 375 mcg estradiol), may be limited by surface area requirements for gel application | $58–$154 |
| Estradiol valerate** Injectable (IM)[f] | 3–4 mg q weekly or 6–8 mg q 2 weeks | Variable[c] | 10mg q weekly | $36–$46 |

** Price quotes are provided by www.pharmacy.ca. The above prices are accurate as of May 2018 and represent the price for a 4-weeks supply of a generic brand of medication unless indicated otherwise (ranging from low dose to maximum dose). Prices include a usual and customary dispensing fee of $9.99, which may vary from pharmacy to pharmacy.* **Note: For patients on ODB, spironolactone, cyproterone, and oral estradiol are covered without the submission of an EAP form.**
*** Estradiol valerate IM must be prepared by a compounding pharmacy, price quote provided by Pace Pharmacy (including $10.99 dispensing fee)*
***a)*** *rarely required or used. Maximal effect does not necessarily require maximal dosing. Use clinical judgement in selecting optimal individual dosing;* ***b)*** *Estradot® brand;* ***c)*** *Usual doses vary significantly between individuals. Use starting doses and titrate up based on patient response. Maximum doses are not often needed. Use clinical judgement in selecting optimal individual dosing;* ***d)*** *200 mcg daily given as 2x100 mcg patches applied twice weekly (4 patches/week);* ***e)*** *Estragel® brand* ***f)*** *Estradiol valerate IM must be prepared by a compounding pharmacy, commonly at the minimum concentration of 10mg/mL. Per updated Ontario guidelines, opened multi-use vials must be discarded after 28 days.*

## SAFETY

Transdermal estradiol seems to be less thrombogenic than oral estradiol with fewer hepatic side effects and is thus recommended for patients over 40 or with risk factors for cardiovascular, thromboembolic, or liver disease.[7]

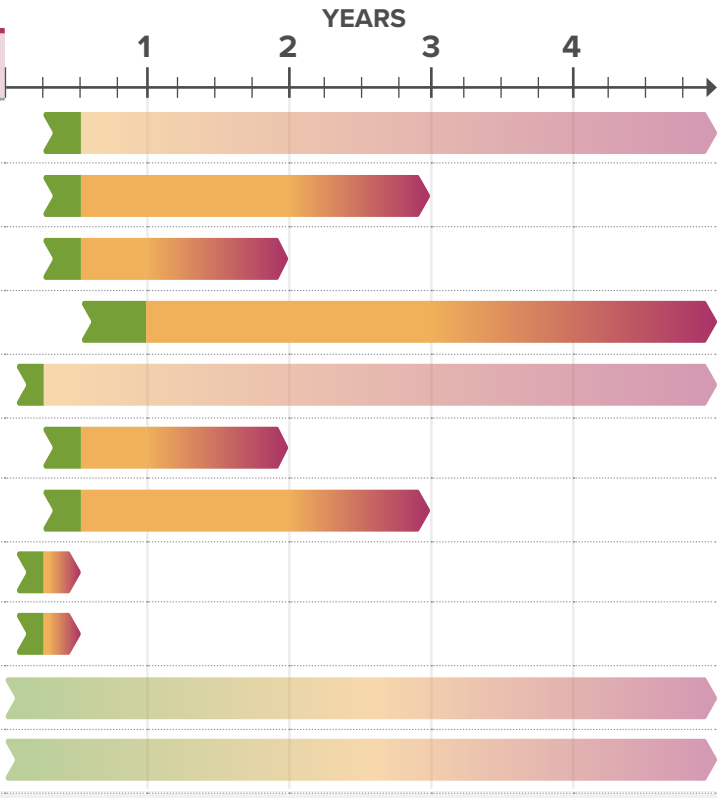
## PREVENTIVE CARE

Transfeminine patients maintained on feminizing hormone therapy have unique preventive care needs and recommendations. An adapted ***Preventive Care Checklist*** for transfeminine patients that can be used at the point of care can be found in the full Guidelines.

## EFFECTS AND EXPECTED TIME COURSE OF FEMINIZING HORMONES

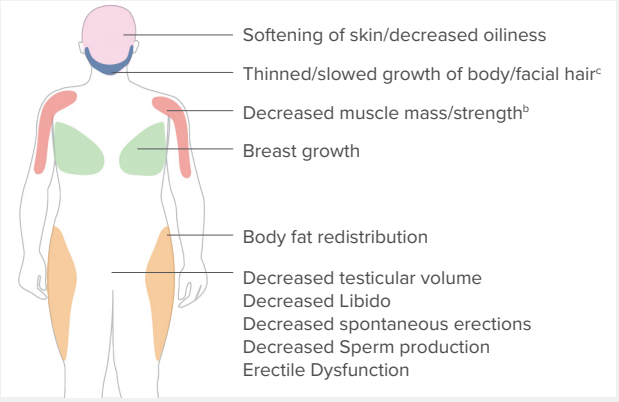
The degree and rate of physical effects are largely dependent on patient-specific factors such as age, genetics, body habitus and lifestyle, and to some extent the dose and route used (selected in accordance with a patient's specific goals and risk profile).[8]

| Physical Effects | Reversibility | Onset[a] | Expected maximal effect[a] |
|---|---|---|---|
| Softening of skin/ decreased oiliness | Reversible | 3-6 months | Unknown |
| Body fat redistribution | Reversible/ Variable | 3-6 months | 2-3 years |
| Decreased muscle mass/strength[b] | Reversible | 3-6 months | 1-2 years |
| Thinned/slowed growth of body/facial hair[c] | Reversible | 6-12 months | >3 years |
| Scalp hair loss (loss stops, no regrowth) | Reversible | 1-3 months | Variable |
| Breast growth | Irreversible | 3-6 months | 1-2 years |
| Decreased testicular volume | Variable | 3-6 months | 2-3 years |
| Decreased libido | Variable | 1-3 months | 3-6 months |
| Decreased spontaneous erections | Variable | 1-3 months | 3-6 months |
| Decreased sperm production | Variable | Variable | Variable |
| Reduced erectile function | Variable | Variable | Variable |




**Keep in mind:** Use patient preferred terminology. "Testicular" and "erections" may be upsetting to some but not all. Physical changes related to androgen blockade and estrogen may take months to appear and are generally considered to be complete after 2-3 years on hormone therapy. Breast growth is an aspect of feminization to which many transfeminine patients assign great importance. The degree of breast development is dependent on many factors, but most transfeminine patients experience modest breast development (average cup size <A, at a developmental Tanner stage of 2-3).[9, 10] Feminizing therapy does not affect the pitch of the voice in transfeminine patients.

*a) Estimates represent unpublished clinical and published observations[11,12,13]*
*b) Significantly dependent on amount of exercise;*
*c) Complete removal of facial hair requires electrolysis, laser treatment, or both*

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*Visual reference: Tetzlaff K.Patient's guide to transgender, trans, & gender diverse health. 2015. https://ktetzlaffdotcom.files.wordpress.com/2015/01/ tetzlaff_transhealthbooklet1.pdf*

## MONITORING STRATEGIES & DOSE ADJUSTMENTS

- Standard monitoring of a feminizing hormone regimen should be employed at baseline, 3, 6, and 12 months; and yearly thereafter (creatinine and electrolytes should be checked 4-6 weeks after the initiation or dose increase of spironolactone).
- Some providers prefer to see patients monthly until an effective dose is established. Follow up visits should include a functional inquiry, targeted physical exam, bloodwork, and health promotion/disease prevention counselling as indicated.
- Dose titration of an anti-androgen and estrogen may be performed over the course of 3-6 months or more and will depend on patient goals, physical response, measured serum hormone levels, and other lab results.
- For many transfeminine patients, the goal will be to achieve the suppression of testosterone into the female range. Hormone levels for those seeking a more androgynous appearance may intentionally be mid-range between male and female norms.
- Measurement of total testosterone is adequate to assess the degree of androgen suppression, without the routine need for free testosterone levels. Be mindful that patients may have clinically relevant results without complete suppression of testosterone because of androgen blockade, which is not measurable.
- Serum estradiol levels should also be monitored. Most patients attain considerable feminization at estradiol levels between 200-500 pmol/L.

**Keep in mind:**
Clinical effects are the goal of therapy, not specific lab values. If the sex marker associated with the patient's health card has not been changed, the reported reference ranges will refer to the sex assigned at birth. Reference ranges vary between laboratories - refer to reference ranges from the specific laboratory (often available online or by request from the lab).

## HORMONE MONITORING SUMMARY FOR TRANSFEMININE PATIENTS

In this table, smaller and lighter grey checkmarks indicate parameters that are measured under particular circumstances.
**NB:** Individual parameters should be considered more frequently if concerns identified or existing risk factors are present.

Non-hormone labs:

- **Hemoglobin/Hematocrit** - use female reference for lower limit of normal and male reference for upper limit of normal
- **Creatinine** - use male reference for upper limit of normal.

| | Baseline | Month 3 | Month 6 | Month 12[e] | Yearly | According to guidelines for cis patients, or provider discretion |
|---|---|---|---|---|---|---|
| Exam/ Investigations | Focused Physical Exam. Include: height, weight, BP, +/- breast inspection/ measurement(s)* | BP, weight, +/- breast inspection/ measurement(s) at 12 months* | | | See Preventive care checklist for transfeminine patients and Accompanying Explanations in the full Guidelines. | |
| **BLOODWORK** | | | | | | |
| CBC[a] | ✓ | ✓ | ✓ | ✓ | ✓ | |
| ALT[b] | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Creatinine/Lytes[c] | ✓ | ✓ | ✓ | ✓ | ✓ | |
| HbA1c or Fasting Glucose | ✓ | | | ✓ | | ✓ |
| Lipid profile | ✓ | | | ✓ | | ✓ |
| Total Testosterone | ✓ | ✓ | ✓ | ✓ | ✓ | |
| Estradiol | ✓ | ✓ | ✓ | ✓ | ✓ | |
| Prolactin[d] | ✓ | | | ✓ | ✓ | ✓ |
| Other | Hep B and C | | | | | |
| | Consider: HIV, syphilis, and other STI screening as indicated, frequency depending on risk | | | | | |

** for patients who may have interest in OHIP-covered breast augmentation surgery, perform breast inspection at baseline and 12 months with particular attention to Tanner stage. Chest circumference at fullest part of the breast and areolar diameter may be helpful in determining the presence or absence of breast growth*
*a) at baseline for all, and regularly with cyproterone*
*b) at baseline for all and regularly with cyproterone, otherwise repeat once at 6-12 months then as needed*
*c) Cr and lytes should be monitored at each visit with spironolactone (including 2-6 weeks after starting), but is only required at baseline and then once between 6-12 months with cyproterone unless risk factors or concerns re: renal disease are present*
*d) Prolactin should be monitored at least yearly with the use of cyproterone, and more frequently if elevation is noted*
*e) during first year of treatment only*

This Quick Reference Guide for pimary care providers was authored by Dr. Amy Bourns and produced by Rainbow Health Ontario, a program of Sherbourne Health, to accompany the ***Guidelines for Gender-Affirming Primary Care with Trans and Non-Binary Patients, 4th edition.***

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