Gender Health SF Gender Affirming Hormone Therapy (GAHT)
Dosing & Monitoring Guide for Primary Care
Updated September 2023

How to use this document:
This document is intended to be a readily accessible dosing and monitoring guide for use within SFDPH. It was compiled after a comprehensive review of existing evidence as of September 2023, and it reflects adaptation of the WPATH SOC8 as well as our combined clinical practice within SFDPH. It is not a comprehensive resource for providing gender affirming primary care. We encourage you to utilize additional resources in the care of trans and gender diverse (TGD) people, such as: WPATH SOC 8, UCSF Guidelines for the Primary and Gender Affirming Care of Transgender and Gender Nonbinary People, Transline, and the Endocrine Society Guidelines.

For Gender Care Consultation & Linkage:
Submit e-Consult to Gender Health SF for questions about providing gender affirming care, hormone therapy and surgery referral, or to link your patient to a comprehensive gender affirming care clinic in our system.

Adolescent & Pediatric Gender Care:
Evidence supports significant improvements in psycho-social outcomes for youth who access gender affirming care. We recommend referring patients between 12 and 18 (and up to age 25) to SFDPH's dedicated pediatric/adolescent gender care clinic, Dimensions Clinic at Castro Mission Health Center by submitting an e-Consult to Gender Health SF. GHSF e-Consult service can also provide consult and linkage for gender care for children under the age of 12. For patients interested in GnRH agonists, you can counsel that labs, multidisciplinary visits and DEXA scans are part of the care plan.

Conceptualizing risks and benefits of gender affirming hormone therapy (GAHT) and adjunctive treatments:
- The primary threat to the health of trans and gender diverse (TGD) people is the well-documented high rates of discrimination and trauma experienced by these communities, and thus the effects of toxic stress associated with transphobia and the socio/economic effects that follow from it.
- Hormone therapy has been found to be overall safe and is an area of ongoing research.
- Mental health and psychosocial outcomes data for those taking hormones are overwhelmingly positive.
- Data comparing health risk to that of someone's assigned sex may not be clinically useful.
- Most risks associated with taking exogenous hormones can be summarized as assuming the usual risks associated with that endogenous hormonal milieu.

Prepared by Danielle Alkov, MD, Leah Warner, FNP, Layla Welborn, FNP and Barry Zevin, MD, SFDPH Gender Health SF, updated September 2023

Hormonal Therapy, Testosterone

<table>
<tr><th>Route</th><th>Dose</th><th>Use & Effects:</th><th>Adverse Effects:</th></tr>
<tr><td>Injectable:
• Testosterone cypionate (cottonseed oil)
• Testosterone enanthate (sesame oil)

Typical concentration: 100 or 200mg/ml</td><td>Low-end: 50-100mg Q2wk or 25-50mg Q1wk
Mid-range: 100mg Q2wk or 50mg Q1wk
High-end: 200mg Q2wks or 100mg Q1wk

Can be administered IM or Sub-Q</td><td rowspan="9"><table><tr><th>Effects (dose dependent)</th><th>Expected onset</th><th>Reversibility</th></tr><tr><td>Facial and body hair growth</td><td>6-12 months</td><td>Permanent</td></tr><tr><td>Increased muscle mass & fat redistribution</td><td>6-12 months</td><td>Reversible</td></tr><tr><td>Deepened voice</td><td>1-6 months</td><td>Permanent</td></tr><tr><td>Menstrual suppression</td><td>1-6 months</td><td>Reversible</td></tr><tr><td>Clitoral enlargement</td><td>1-6 months</td><td>Permanent</td></tr><tr><td>Acne</td><td>1-6 months</td><td>Reversible</td></tr><tr><td>Androgenic alopecia</td><td>6-12 months</td><td>Permanent</td></tr><tr><td>Mood Changes (improved mood or irritability) and Changes in libido</td><td>Immediate and ongoing</td><td>Reversible</td></tr><tr><td>Genital changes (atrophy, decreased lubrication, microbiome shifts)</td><td>1-6 months</td><td>Partially reversible</td></tr></table></td><td rowspan="9">Adverse effects: ↑weight (may be more lean body mass), oily skin, acne, vaginal atrophy, androgenic alopecia, ↓ HDL cholesterol level, erythrocytosis, androgenization of partners exposed to topical preparations, cardiovascular risk appears to be increased but data lacking and best practice to work to mitigate lifestyle factors. No conclusive evidence of liver dysfunction or impact on blood sugar exists.

Fertility:
Limited evidence on fertility; anecdotal evidence & expert opinion supports that fertility effects are largely reversible. Can consider cryobanking but not generally a covered benefit at this time.

Absolute contraindications:
- Pregnancy
- Testosterone-dependent cancer</td></tr>
<tr><td>Long-acting injectable:
• Testosterone Undecanoate</td><td>750 mg IM q10-14 weeks after loading dose

Rare pulmonary oil microembolism leading to a transient cough; requires injection admin in health care setting by trained professional w/ 30min monitoring afterwards</td></tr>
<tr><td>Topical (Gel):
• Testim
• Androgel 1%
• Androgel 1.62%
• [Androderm and Axiron out of production]</td><td>Low-end: 20-62.5mg every morning Mid-range: 50mg-81 mg every morning
High-end: 100mg every morning Dispensed as:
Testim 50mg/5g, 2.5g-5g
Androgel 1%, 12.5mg/actuation
Androgel 1.62%, 20.25mg/actuation</td></tr>
<tr><td>Oral:
• Testosterone Undecanoate (Jatenzo)</td><td>158-396 mg BID must take with fatty foods</td></tr>
<tr><td>Subdermal (pellets):
• Testopel</td><td>150-600 mg every 3-6 months subcutaneous surgical administration (referral UCSF Urology)</td></tr>
<tr><td>Intranasal:
• Natesto</td><td>11 mg TID
Not currently on MediCal formulary</td></tr>
</table>

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Lab Monitoring for Patients Starting/On Testosterone

Testosterone	Hemoglobin/Hematocrit	Other, based on risk factors
- No baseline - 3mo after starting or dose change - PRN for clinical concern - Testosterone monitoring can be complex. If total testosterone level does not correlate with clinical picture, consider ordering SHBG and calculating bio-available testosterone. - Early AM T level not necessary for transmasc pts (lab recommendation based on person with natal testes)	- Baseline (no need to delay prescription) - 3mo after starting or dose increase - Annually thereafter - Anticipate Hgb/Hct to ^ to physiologic male range	- A1c - Fasting lipids - LFTs - Pregnancy test

Notes on testosterone therapy:

Choosing a formulation:

- Choice of testosterone is individualized based on patient needs, availability, co-morbid conditions, and adverse effect profile:

Injectable ○ Testosterone can be administered every 2 weeks for convenience, however some patients experience adverse mood effects due to fluctuations in blood testosterone levels with Q2week injections.

- ○ May be administered weekly for more stable blood testosterone levels. ○ SubQ thought to have more stable absorption and release into circulation and may require slightly lower dosing to achieve therapeutic serum levels of testosterone compared to IM injections.
- ○ SubQ vs IM administration based on patient preference for injection site, needle size, liquid volume, frequency of administration and stability of hormone levels.

Topical ○ Topical testosterones achieve more physiological daily levels, but some patients do not have adequate effects. ○ May be used for slower changes or to maintain effects after achieving desired effects with other formulations. ○ Risk of exposure of others to testosterone. Important to allow adequate drying time. ○ Testosterone ointment, cream, or gels have been used topically applied directly to facial and body areas and clitoris to promote hair growth and clitoral growth however all information about effectiveness is anecdotal. Topically applied testosterone is absorbed systemically & should be included in total patient dose; decreased dosing of other testosterone is recommended.

Dose adjustment:

- Adjust dosing based on patient reported changes and satisfaction in meeting their embodiment goals, and with lab monitoring of testosterone. Changes can take months to occur. When levels are too high, aromatization to estradiol can occur.

Preventive care related to testosterone therapy:

- Continue testosterone even after maximum body changes to prevent osteoporosis after oophorectomy.
- Strongly encourage and assist patients with smoking cessation to decrease cardiovascular risk.
- For managing unanticipated bleeding after period of amenorrhea for a person taking testosterone, first evaluate adherence and testosterone levels, if any concern then work-up as AUB.

Sexual health related to testosterone therapy:

- Assess for safer sex practices and effects on sexual behavior after beginning testosterone.
- Testosterone is not a contraceptive; educate patient to use contraception if having sex that could result in pregnancy
- Counsel on impact on fertility

Medication interactions:

- Changes in anticoagulant activity may be seen in pts on warfarin, more frequent INR monitoring may be needed.
- Changes in insulin sensitivity or glycemic control may occur in people with diabetes

Hormonal Therapy, Estrogen

Route	Dosing	Use and Effects:			Adverse Effects:
		Effects (dose dependent)	Expected Onset	Reversibility	↑weight most likely due to total body fat changes, ↑risk DVT & PE (increased for age above 40, cigarette smokers, highly sedentary, obese & those w/ underlying thrombophyllic disorders), decrease in sexually stimulated erections, migraine/headache, melasma, skin irritation w/ patch. Evidence on CV risks and benefits are mixed and studies are ongoing. Best practice is to counsel on individual risk factors to enhance cardiovascular health. **Fertility:** Limited evidence on fertility but known to decrease sperm motility and count and extent reversible unknown. Can consider cryobanking; not generally a covered benefit at this time.
Oral: • Estradiol PO (micronized, Estrace) • Estradiol SL	Low-end: 2mg/day Mid: 4mg/day High-end: 6mg/day	Skin softening	3-6 months	Reversible	
		Body fat redistribution and decreased muscle mass	3-6 months	Reversible	
		Breast Development	3-6 months	Irreversible	
IM/SubQ: • Estradiol valerate (Delestrogen)(typical concentrations: 20mg/ml, 40mg/ml), castor oil • Estradiol cypionate (Depo-estradiol) (concentration: 5mg/mL), cottonseed oil	Low-end: 5mg Q2wk/ 2mg Q1wk Mid-range: 10-20mg- Q2wk/ 5-10mg Q1wk High-end: 30mg Q2wk/ 15mg Q1wk	Decreased testicular volume	3-6 months	Irreversible	
		Decreased spontaneous erections	1-3 months	Reversible	
		Libido changes	1-3 months	Reversible	
		Mood changes (improved mood or mood fluctuations)	Immediate & ongoing	Reversible	
Topical, Patch: • Climara, Menostar—weekly; Minivelle, Vivelle-Dot—twice weekly	Low-end: 0.025-0.5mg/24hr Mid-range 0.1mg/24hr High-end: 0.2mg/24hr*				
Topical, Gel: • Divigel, Elestrin, Estrogel	0.025-0.2mg/day				

** In our clinical practice at SFDPH, we are comfortable using higher doses of the patch to meet patient goals (up to double those listed above from SOC8) if serum estradiol levels remain in physiologic range.*

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Lab Monitoring for Patients Starting/On Hormone Therapy with Estrogen, Spironolactone

Interpreting labs: use upper limit of physiologic female range estradiol and usual female range testosterone, in combination with patient-specific goals, to guide dosing. These labs are intended in addition to those appropriate for patients' age & medical conditions. Usual primary care screening guidelines for all people apply.

Medication	Estradiol	Testosterone	BUN / SCr, Electrolytes
Estrogen	- No baseline - 3mo after starting or dose change	-No baseline -3mo after starting or dose change as consistent with patient goals	
Spironolactone		- Optional 3mo after starting as consistent with patient goals	- Baseline - 2 weeks after starting or ↑dose - Consider closer monitoring in elderly, renal dysfunction, other high risk pts or possible drug interactions - Every 12mo on stable dose

Notes on estrogen therapy:

Choosing a formulation:

- Choice of estrogen is individualized based on patient needs, availability, co-morbid conditions, and adverse effect profile:

  Oral
  - Avoid ethinyl estradiol due to significantly increased CV risk
  - Avoid conjugated equine estrogens (↑CV risks, difficult to monitor & serious ethical concerns as obtained from urine of immobilized catheterized pregnant horses)

  Topical
  - Skin irritation can be a problem with patches and switching the type of patch may help.

  Injectable
  - Benefit of weekly dosing is greater stability of hormone levels, particularly important if mood swings or other symptoms occur with Q2W dosing.
  - Estradiol cypionate (depo-estradiol) has the longest half-life of any of the injectable estrogens and may be appropriate for patients who need less frequent injecting or have trouble with mood fluctuations or other symptoms at the start or end of the injection cycle. Dose adjustment:

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- Prescribe low dose for patients based on patient goals, or for cigarette smokers and others at high risk of thrombosis, patients with uncontrolled diabetes and/or metabolic syndrome and/or active cardiovascular disease.
- Prescribe higher doses as needed based on clinical goals, response, smoking cessation, stabilization of co-morbid conditions.

- For those seeking to maximize effects, doses should be reduced after maximum effects have occurred (usually after 2-4 years). Some advocate routinely decreasing after 2 years. Consider reducing after gender affirming surgery (orchiectomy, vaginoplasty, mammoplasty, etc) based on patient goals.

<u>Preventive care related to estrogen therapy:</u>

- Continue estrogen even after maximum body changes to prevent osteoporosis and to maintain effects in those s/p gonadectomy.
- Recommended doses for "maintenance" hormone therapy for patients on effective anti-androgen doses or post gonadectomy have not been defined but doses recommended for post-menopausal prevention of osteoporosis or the starting doses above have been suggested.

Additional Medications Used in Gender Care

Medication	Dose	Use & Effects	Adverse Effects
Spironolactone	Low-end: 25-50mg BID Mid-range: 50mg BID High-end: 150mg BID	Anti-androgen therapy Unnecessary after orchiectomy ↓erections Mild breast growth (irreversible) ↓facial and body hair growth ↓libido ↓BPH	Mild diuretic Hyperkalemia Excretion of Na, Ca, Cl Impotence Interactions: ACEi ARB TMP-SMX K-sparing diuretics
5 alpha reductase inhibitors	Finasteride: Low-end: 1mg daily High-end: 5mg daily Dutasteride: 0.5 mg daily	Anti-androgen therapy Decreases levels of dihydrotestosterone. In patients on testosterone, can treat androgenic alopecia but unclear how it can impact virilization. For patients on estradiol, can help preserve erections and can facilitate hair growth.	In person with uterus: can cause cramping and spotting. Often 1mg dose not covered by insurance but 5 mg dose is covered.
Progesterone	Micronized progesterone (natural): 100-200mg QHS Medroxy-progesterone (synthetic): 5-10mg PO daily Depo-provera: 150mg IM Q3mo	For patients seeking breast development, anecdotal reports of enhanced breast contour and nipple development. Aecdotal reports of enhanced libido. Consider limiting use to 12mo. For patients with a uterus, Depo-provera (and other progesterone-based forms of birth control) can be used for contraception and cessation of menses.	Weight gain, mood changes May also have androgenizing affects including hair growth, acne Beyond one year, may increase risk CVD
Minoxidil	Topical 5% Oral 1.25-5 mg daily	Increases hair growth Does not interact with hormonal therapy	Hypertrichosis Hypotension Toxic to cats Edema Cardiovascular

GnRH agonist	Histrelin Acetate 50 mg SQ implant (labeled for 1 year ,effective for 2) Leuprolide acetate 3.75–7.50mg SQ/IM monthly or 11.25/22.5mg SQ/IM 3/6 monthly Triptorelin (Triptodur): 22.5 mg IM 6 month	Suppresses body's endogenous production of sex hormones; very effective in hormonal blockade	Can impact bone heath if no sex steroid in system. Initial rise in endogenous sex hormone occurs.

Phosphodiesterase inhibitors	Tadalafil: 5-20 mg PO PRN Sildenafil 25-100 mg PO PRN	For patients on estrogen or androgen blockers wanting to maintain erections	Priapism
Selective estrogen receptor modulators (SERMs)	Tamoxifen, raloxifene	Theoretical potential to cause body fat redistribution without breast development. At the time of this writing, none of the authors have prescribed SERMs but we are aware of increasing use among non-binary patients seeking to avoid breast development.	Risk of DVT/PE/CVA in folks taking it for breast cancer

*Bicalutamide – At the time of this writing, none of the authors use this medication due to potential for hepatoxicity and we can generally get safer alternatives covered by insurance. Use caution and avoid in G6PD, increased risk of methemoglobinemia, taking other heptotoxic substances