

TRANSGENDER MEDICAL CONSULTATION SERVICE

# TRANSLINE

## GENDER AFFIRMING HORMONE THERAPY

### PRESCRIBER GUIDELINES

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health services **LYON MARTIN**  
a program of healthRIGHT 360



PROJECT  
**HEALTH**  
HARNESSING EDUCATION,  
ADVOCACY & LEADERSHIP  
FOR TRANSGENDER HEALTH

# Gender Affirming Hormone Therapy Guidelines



## What is TransLine?

- Modeled after the National Clinician Consultation Center for HIV at UCSF, TransLine is a national e-consultation service aiming to increase provider competence and confidence in caring for transgender patients by providing an easily accessible online clinical support tool. All consultation questions are answered by a vetted expert in transgender health within two business days.
- Log on at <https://transline.zendesk.com>

## Who is TransLine?

- Launched in 2012 by Lyon-Martin Health Services (San Francisco), TransLine established a collaborative partnership with trans health experts at Fenway Health (Boston), Mazzoni Center (Philadelphia), and Baystate Health (Northampton) in late 2013. Additional providers from Chase Brexton (Baltimore) and Howard Brown (Chicago) were on-boarded in 2017. All partnering providers participate on a rotating “on-call” schedule to answer incoming e-consultation requests.
- Lyon-Martin remains the organizational lead and clearing-house for all consultation requests, routing questions to the appropriate on-call provider and ensuring quality and timeliness of responses.

## Why create hormone therapy prescriber guidelines?

- We sought to create a national standardized guideline of best practices in hormone therapy provision as a reference to achieve uniformity in our answers because we observed that even experts in trans care provided different responses to similar questions posed. This is largely due to the disparate recommendations given in each clinic’s protocol and the general lack of research supporting hard and fast rules when it comes to hormone prescribing for gender transition. We reconciled all the different protocols published to date and sought input from other nationally acclaimed experts in transgender care to contribute to our guidelines. Due to the lack of research on the long-term effects of hormone therapy in transgender people, many of our suggestions are based on low-level evidence in cis-gender populations and our aggregated collective knowledge derived from clinical practice and experience. Acknowledging that gaps in evidence exist, differences in practice will continue to be reasonable and expected until hard evidence provides answers.
- Our first meeting on hormone protocol standardization took place at The Inaugural USPATH Conference in 2017 and included additional expert clinicians from Callen-Lorde Community Health Center (New York City), The LA LGBT Center (Los Angeles), Whitman-Walker (Washington DC), Apicha Community Health Center (New York City), API Wellness Center (San Francisco), Legacy Community Health (Houston), and Care Resource (Miami). Since then we have continued to meet via conference call to create this guideline to inform our answers to TransLine consultation requests.

## A special thank you to all who contributed to this document:

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# Gender Affirming Hormone Therapy Guidelines

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## Trans Masculine: Exogenous Testosterone Dosing

Medication	Start/Usual Dose	Typical Max Dose	Frequency	Pros	Cons	Notes
<b>Intramuscular or Subcutaneous<sup>1</sup> Testosterone</b>  (Testosterone Cypionate or Testosterone Enanthate)	50mg – 80mg  (0.25mL - 0.4mL of 200mg/mL solution or 0.5mL - 1.0mL of 100mg/mL solution)	100mg  (0.5mL of 200mg/mL solution)	Weekly <sup>2</sup>	<ul style="list-style-type: none"> <li>Less frequent administration compared with transdermal</li> <li>Peak of injectable may better suppress endogenous hormone production</li> </ul>	<ul style="list-style-type: none"> <li>Peak/trough fluctuation effect</li> <li>Self-injection or frequent in-office injections</li> <li>Needle use</li> </ul>	<ul style="list-style-type: none"> <li>Cypionate formulated in cottonseed oil (use if allergic to sesame)</li> <li>Enanthate formulated in sesame oil (use if allergic to cottonseed)</li> <li>Enanthate has slightly shorter half-life than cypionate</li> </ul>
<b>Transdermal Testosterone Topical Gel</b>  (AndroGel, Axiron, Testim)	20mg – 62.5mg  <ul style="list-style-type: none"> <li>AndroGel 1%, 12.5mg/actuation, 2-5 pumps</li> <li>AndroGel 1.62%, 20.25mg/actuation, 1-3 pumps</li> <li>Axiron, 30mg/actuation, 1-2 pumps</li> <li>Testim, 50mg/5g, 2.5g-5g</li> </ul>	100mg  <ul style="list-style-type: none"> <li>AndroGel 1%, 12.5mg/actuation, 8 pumps</li> <li>AndroGel 1.62%, 20.25mg/actuation, 5 pumps</li> <li>Axiron, 30mg/actuation, 3 pumps</li> <li>Testim, 50mg/5g, 10 g</li> </ul>	Daily	<ul style="list-style-type: none"> <li>No needle use</li> <li>Less fluctuation in levels</li> <li>Good for more gradual effects</li> </ul>	<ul style="list-style-type: none"> <li>Slower to stop menses and may not fully stop at lower doses</li> <li>Risk of transferring to others/pets so must instruct how to apply per package insert</li> <li>Some products are scented and may not be appropriate for those with scent-sensitivities</li> <li>Daily application</li> <li>May be expensive if not covered by insurance</li> </ul>	
<b>Transdermal Testosterone Patch</b>  (Androderm)	2mg – 6mg  (1 - 3x 2mg patches)	8mg  (2x 4mg patches)	Daily	<ul style="list-style-type: none"> <li>No needle use</li> <li>Less fluctuation in levels</li> <li>Good for more gradual effects</li> <li>Less risk of transfer to others (compared to the topical transdermal)</li> </ul>	<ul style="list-style-type: none"> <li>Slower to stop menses and may not fully stop at lower doses</li> <li>Adhesive irritation, can fall off with sweat<sup>3</sup></li> <li>Daily application</li> <li>May be expensive if not covered by insurance</li> </ul>	
<b>Testosterone Pellets</b>  (Testopel)	450mg – 600mg  (6 - 8x 75mg pellets)	750mg  (10x 75 mg pellets)	Every 3-4 months	<ul style="list-style-type: none"> <li>No needle use</li> <li>Less frequent administration</li> <li>Less fluctuation in levels</li> </ul>	<ul style="list-style-type: none"> <li>More invasive, requires minor surgery to implant</li> <li>May be expensive if not covered by insurance</li> </ul>	<ul style="list-style-type: none"> <li>Lab draw frequency: Baseline draw prior to starting, Once at 1 month, then at 3 months prior to next insertion</li> </ul>
<b>Testosterone Undecanoate IM</b>  (Aveed)	750mg  (3mL of 750mg/3mL solution)	N/A	Initial injection, at 4 weeks, then every 10 weeks thereafter	<ul style="list-style-type: none"> <li>Less frequent injection</li> <li>Less fluctuation in levels</li> </ul>	<ul style="list-style-type: none"> <li>Pulmonary oil embolism risk</li> <li>PCP and facility need registration</li> <li>May be expensive and unlikely to be covered by insurance at present</li> </ul>	<ul style="list-style-type: none"> <li>Formulated in castor oil</li> </ul>
<b>Testosterone Undecanoate Oral</b>  (Jatenzo)	316mg – 474mg  (1x 158mg capsules BID 1x 198mg capsules BID 1x 237mg capsules BID)	790mg  (1x 158mg + 1x 237mg capsules BID)	Daily	<ul style="list-style-type: none"> <li>No needle use</li> <li>Less fluctuation in levels</li> </ul>	<ul style="list-style-type: none"> <li>First pass metabolism</li> <li>Daily dose</li> </ul>	<ul style="list-style-type: none"> <li>Recommend divided doses (BID) to decrease first pass effect and hepatotoxicity.</li> <li>Starting dose 237mg BID, then adjust dose to min of 158mg BID, with a max of 395mg BID</li> </ul>
<b>Testosterone Nasal Gel</b>  (Natesto)	33mg  (2 pump actuations, one 5.5mg actuation per nostril = 11mg, TID)	N/A	Daily	<ul style="list-style-type: none"> <li>No needle use</li> <li>Less fluctuation in levels</li> </ul>	<ul style="list-style-type: none"> <li>Administration three times per day</li> </ul>	<ul style="list-style-type: none"> <li>Not recommended for use with other nasally administered drugs other than sympathomimetic decongestants</li> </ul>

<sup>1</sup> Testosterone Cypionate/Enanthate and Estradiol Valerate/Cypionate are FDA approved for delivery only through intramuscular injections. However, for many patients, subcutaneous injection serves as a safe and effective alternative option due to decreased pain with injection. There are limited studies supporting subcutaneous delivery, but anecdotally, some patients and providers prefer this method. There is a caveat that hormone level may be more variable due to variable absorption, and, for those with thicker adipose tissue, it may take a longer time to achieve steady state.

<sup>2</sup> For injectable can alter dose to every 10 or 14 day regimen if preferred

<sup>3</sup> To diminish irritation, apply 1% hydrocortisone to patch area for 1 hour duration before, then clean area, prior to patch application. Tincture of benzoin applied to patch area will promote adhesion.

# Gender Affirming Hormone Therapy Guidelines

## Testosterone Formulations: Approximate Dose Equivalent Chart

Injectable	Transdermal Patch	Transdermal Gel	Pellets
50mg weekly (0.25mL of 200mg/mL solution weekly)	2-4mg	20-50mg	375mg (5x 75mg pellets)
80mg weekly (0.4mL of 200mg/mL solution weekly)	6mg	50-75mg	525mg (7x 75mg pellets)
100mg weekly (0.5mL of 200mg/mL solution weekly)	8mg	75-100mg	750mg (10x 75mg pellets)
125mg weekly (1mL of 200mg/mL solution)			900mg (12x 75mg pellets)

## Trans Masculine: Medications to Supplement Testosterone

Medication	Start/Usual	Typical Max	Frequency	Pros	Cons	Notes
<b>Finasteride Oral</b> (Proscar, Propecia)	1mg (¼ of 5 mg pill or 1x 1mg pill)	5mg (1x 5mg pill)	Daily	<ul style="list-style-type: none"> <li>Prevent or slow balding due to androgenic alopecia</li> </ul>	<ul style="list-style-type: none"> <li>May slow other DHT-dependent changes like secondary hair growth and clitoral growth, so this should be discussed with patients, especially if considering using at the beginning of testosterone use, unless they are deliberately trying to prevent above mentioned changes</li> </ul>	<ul style="list-style-type: none"> <li>5mg are cheaper than 1mg, can split 5 mg into quarters</li> </ul>
<b>Dutasteride Oral</b> (Avodart)	0.5mg (1x 0.5mg tablet)	0.5mg (1x 0.5mg tablet)	Every 3 days	<ul style="list-style-type: none"> <li>Slows and prevents balding due to androgenic alopecia</li> <li>Can take every 3 days rather than every day with Finasteride</li> </ul>	<ul style="list-style-type: none"> <li>Same as Finasteride Cons</li> </ul>	
<b>Compounded Testosterone Cream</b> (applied to genitals)	12.5mg –50mg <sup>4</sup> (0.25g –1g of 5% cream)	100mg (2g of 5% cream or 1g of 10% cream)	Daily	<ul style="list-style-type: none"> <li>Clitoral enlargement</li> <li>Can also be used as a cheaper transdermal alternative to Androge</li> </ul>	<ul style="list-style-type: none"> <li>May worsen balding due to androgenic alopecia</li> </ul>	<ul style="list-style-type: none"> <li>Some surgeons may suggest the topical application of testosterone to the clitoris as an adjunct to growth. There is no definitive evidence for this practice; however if undertaken, the applied dose should be subtracted from the client's total testosterone dosage (if it is used in addition to another formulation of T). Contact compounding pharmacy to determine equivalent amount to be subtracted from total dose, as equivalency depends greatly on what chemicals testosterone is compounded with. Long-term efficacy is not well established.</li> </ul>
<b>Compounded Dihydrotestosterone (DHT) Cream</b> (applied to genitals)	6mg over course of day 20mg of 10% cream	6mg over course of day 20mg of 10% cream	Apply 2mg 3x per day	<ul style="list-style-type: none"> <li>Clitoral enlargement</li> </ul>	<ul style="list-style-type: none"> <li>May worsen balding due to androgenic alopecia</li> </ul>	<ul style="list-style-type: none"> <li>Same as Compounded Testosterone Cream Notes</li> <li>Not sold or FDA approved in the US, very expensive, and illegal to import due to being a schedule III drug.</li> <li>Overseas this is available as an alcohol-based gel, which, when used on mucous membranes can result in a burning sensation after topical application.</li> </ul>
<b>Leuprolide Acetate IM</b> (Lupron, Eligard)	11.25mg (1 IM shot of 1.25mg/1.5mL dilutant)	22.5mg (2 IM shots of 11.25mg/1.5mL dilutant)	Every 3 months	<ul style="list-style-type: none"> <li>GnRH receptor agonist, very effective to suppress endogenous hormone production</li> <li>Typically only used for teens for puberty suppression; can use either alone or with exogenous hormones</li> </ul>	<ul style="list-style-type: none"> <li>May be expensive if not covered by insurance</li> <li>Not ideal for long-term use due to bone density loss<sup>5</sup></li> </ul>	
<b>Vaginal Estradiol</b> (Estrace, Premarin, Estring, Vagifem)	Dosing same as post-menopausal cis-women	N/A	N/A	<ul style="list-style-type: none"> <li>Treats vaginal atrophy, pain with penetration and unsatisfactory cytology result on pap smear</li> </ul>		<ul style="list-style-type: none"> <li>If just used in preparation for vaginal exam and/or pap smear, short two week course prior can help with pain during exam as well as obtaining satisfactory cytology</li> <li>Approach discussion with sensitivity as some may not feel comfortable using estrogen due to gender dysphoria</li> </ul>

<sup>4</sup> Dosing depends on compounded formulation. Consult with pharmacy to determine usual cis-gender male replacement dose and start at approximately 25-50% of that dose.

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<b>Medroxyprogesterone Acetate IM (Depo-Provera)</b>	150mg (1mL of 150mg/mL solution)	150mg (1mL of 150mg/mL solution)	Every 3 months	<ul style="list-style-type: none"> <li>Stops persistent vaginal bleeding on T<sup>5</sup></li> <li>Contraception</li> </ul>		<ul style="list-style-type: none"> <li>3 month course, then re-evaluate</li> </ul>
<b>Medroxyprogesterone Oral (Provera)</b>	5mg (1 5mg tablet daily)	10mg (1 10mg tablet daily)	Daily	<ul style="list-style-type: none"> <li>Stops persistent vaginal bleeding on T<sup>5</sup></li> </ul>		<ul style="list-style-type: none"> <li>Short 7-10 day course to as long as a 3 month course</li> </ul>
<b>Anastrozole (Arimidex)</b>	1mg	1mg	Daily	<ul style="list-style-type: none"> <li>Stops persistent vaginal bleeding on T<sup>5</sup></li> </ul>	<ul style="list-style-type: none"> <li>Not ideal for long-term use due to bone density loss<sup>6</sup></li> </ul>	<ul style="list-style-type: none"> <li>3 month course</li> <li>May cause menopausal symptoms</li> </ul>
<b>Levonorgestrel Intrauterine Device (Mirena, Skyla, Kyleena)</b>	20mcg/day (Mirena) 14mcg/day (Skyla) 19.5mg/day (Kyleena)	N/A	N/A	<ul style="list-style-type: none"> <li>Stops persistent vaginal bleeding on T<sup>5</sup></li> <li>Contraception</li> </ul>		<ul style="list-style-type: none"> <li>Mirena lasts 5 years</li> <li>Skyla lasts 3 years</li> <li>Kyleena lasts 4 years</li> </ul>

## Trans Masculine: Exogenous Testosterone Monitoring

This is in addition to any PCP visits or lab work indicated to monitor other health risks, disease states or standard medical screening.

Baseline	Once Amenorrheic (or 2-3 months after start)	After change in dose (1-3 months after change)	6 months after first achieving maintenance dose (OPTIONAL, esp if otherwise young and healthy)	12 months after achieving stable maintenance dose (unless other concerns)	When to draw testosterone?
CBC, CMP	Testosterone (total)	Testosterone (total)	CBC, Testosterone (total)	CBC, Testosterone (total), CMP*, Lipids**	Injectable: One week after injection <sup>7</sup>  Transdermal: Trough (don't apply it on the day of the draw, or wear gloves when administering on day of draw to avoid contaminating sample)  Oral: 6 hours after morning dose at least 7 days after starting or adjusting dose
PCP exam, BP, UPT*	PCP check-in & BP	PCP check-in & BP	PCP check-in & BP	PCP check-in & BP	

\*Only if at risk for pregnancy

\*\*In all patients, check lipids one time at 12 months after starting, and repeat every 12 months if there is a concern of fatty liver, chronic liver disease, high cholesterol, otherwise ok to just check once.

### Total Testosterone Reference Range:

- Use cisgender male suggested reference range. Reference ranges may vary depending on lab.
- The goal is to be around or below mid-normal range for a cisgender male, but also it depends on transition goals of the client
- If testosterone is supraphysiologic, before making major adjustments, review administration technique to ensure correct dosing and re-check level. If persistently supraphysiologic, decrease dose and re-check again.
- Recommended mid-cycle draw reference ranges vary:
  - Fenway: 300-700ng/dl
  - Endocrine Society: 400-700ng/dl
  - UCSF's 350-1100ng/dl unless in setting of symptoms like migraines, pelvic cramping or mood swings in which case recommends peak and trough draw may be helpful. If supraphysiologic, consider change to transdermal or decreasing injection interval

### Secondary Polycythemia

- Use CBC reference range for cisgender men
- Hematocrit <54 is ideal
- >54 indicates polycythemia, which increases the risk of hypertension and thrombosis
- First rule out pulmonary disease cause such as asthma, smoking, COPD, etc, or JAK2 mutation. EPO level can also be checked to determine if it's primary or secondary polycythemia.
- If polycythemia is actually secondary to testosterone use, there are a few treatment options to choose from other than just decreasing the dose. Since H/H elevation is often due to high peaks of testosterone with injectable, consider:
  - Changing to weekly injection schedule if currently on an every two week injection schedule
  - Changing from injectable to transdermal
  - Stay on current dose/formulation and do therapeutic phlebotomy
- Re-check labs for normalization 1-3 months after change is made

<sup>5</sup> First rule out if testosterone usage has been variable; if T level to high (and aromatizing to E) or T level too low. Persistent vaginal bleeding while on testosterone requires work-up if >12 months amenorrheic

<sup>6</sup> If using Anastrozole or Leuprolide Acetate, in the presence of other risk factors for osteoporosis, consider DEXA scan after 2 years of use

<sup>7</sup> Level will be higher if on every 10 or 14 day dosing than on every 7 day dosing. Doesn't really matter when you draw testosterone, just need to know if it's trough, mid-level, or peak so can determine if the result is where expected to be.

# Gender Affirming Hormone Therapy Guidelines

## Trans Feminine: Exogenous Estrogen Dosing

Medication	Start/Usual Dose	Typical Max Dose	Frequency	Pros	Cons	Notes
<b>Intramuscular or Subcutaneous<sup>1</sup></b> (Estradiol Valerate = Delestrogen or Estradiol Cypionate = Depo-Estradiol)	Valerate: 5mg - 10mg (0.25mL – 0.5mL of 20mg/mL solution)  Cypionate: 1.25mg - 2.5mg (0.25mL – 0.5mL of 5mg/mL solution)	Valerate: 20mg (1mL of 20mg/mL solution or 0.5mL of 40mg/mL solution)  Cypionate: 5mg (1mL of 5mg/mL solution)	Weekly <sup>2</sup>	<ul style="list-style-type: none"> <li>Less frequent administration</li> <li>Systemic effect, avoids first pass effect on liver; however when at peak circulating levels of estrogen, amount delivered to liver may be higher than other modes of delivery</li> <li>Peak of injectable may help better suppress endogenous hormone production</li> </ul>	<ul style="list-style-type: none"> <li>Peak/trough fluctuation effect</li> <li>Self-injection or frequent in-office injections</li> <li>Needle Use</li> </ul>	<ul style="list-style-type: none"> <li>Valerate formulated in castor oil (use if allergic to cottonseed) and is typically used with weekly dosing. The national shortages of the injectable formulation, especially generic Estradiol Valerate, from August 2016 through the finalization of this protocol have made availability sporadic.</li> <li>Cypionate is formulated in cottonseed oil (use if allergic to castor oil) and is typically a quarter of the dose of valerate and can be given at every two week intervals rather than weekly due to the longer half life.</li> </ul>
<b>Estradiol Patch</b> (Vivelle Dot)	0.1mg - 0.2mg  (1-2x 0.1mg patches)	0.4mg  (4x 0.1mg patches)	Bi-weekly or per manufacturers recommendation	<ul style="list-style-type: none"> <li>No needle use</li> <li>Less fluctuation in levels</li> <li>No first pass metabolism</li> </ul>	<ul style="list-style-type: none"> <li>Adhesive irritation, can fall off with sweat<sup>3</sup></li> <li>Daily application</li> <li>May be expensive if not covered by insurance</li> </ul>	<ul style="list-style-type: none"> <li>Preferred method for those with increased risk of DVT/PE/CVD</li> <li>For those who have had DVT/PE/CVD, shared clinical decision-making to resume low-dose (0.05mg) transdermal estrogen may be done, but it should be administered with continuous anticoagulation.</li> </ul>
<b>Estradiol Oral</b> (Estrace)	2mg - 6mg  (1-3x 2mg tablet)	8mg  (4x 2mg tablets daily)	Daily	<ul style="list-style-type: none"> <li>No needle use</li> <li>Less fluctuation in levels</li> </ul>	<ul style="list-style-type: none"> <li>Daily dose</li> <li>First pass metabolism</li> </ul>	<ul style="list-style-type: none"> <li>Single or divided doses dependent on preference; if on higher dose of 6-8mg, would recommend dividing to decrease first pass and hepatotoxicity.</li> <li>Some providers recommend sublingual administration to attempt to bypass first pass metabolism, but it is unclear how much is actually absorbed sublingually vs. swallowed.</li> <li>Consider switch to injectable if not seeing results with oral.</li> </ul>
<b>Premarin Oral</b>	1.25mg - 2.5mg  (1-2x of 1.25mg tablet)	5mg  (4x 1.25mg tablets daily)	Daily	<ul style="list-style-type: none"> <li>No needle use</li> <li>Less fluctuation in levels</li> </ul>	<ul style="list-style-type: none"> <li>Daily dose</li> <li>Rarely used &amp; not preferred due to higher thrombogenic risk compared to estradiol</li> <li>Difficult to monitor estrogen level as it may not reflect true serum levels related to dose.</li> <li>May be expensive if not covered by insurance</li> <li>First pass metabolism</li> </ul>	<ul style="list-style-type: none"> <li>See Estradiol (Estrace) Notes</li> </ul>

## Estrogen Formulations: Approximate Dose Equivalent Chart

Injectable Estradiol Valerate	Injectable Estradiol Cypionate	Transdermal Patch	Oral Estradiol	Premarin
5mg weekly (0.25mL of 20mg/mL solution)	1.25mg weekly (0.25mL of 5mg/mL solution)	0.1mg	2mg	1.25mg
10mg weekly (0.5mL of 20mg/mL solution)	2.5mg weekly (0.5mL of 5mg/mL solution)	0.2mg	4mg	2.5mg
20mg weekly (0.5mL of 40mg/mL solution)	5mg weekly (1mL of 5mg/mL solution)	0.4mg	8mg	5mg

# Gender Affirming Hormone Therapy Guidelines

## Trans Feminine: Medications to Supplement Estrogen

Anti-Androgens	Start/Usual Dose	Typical Max Dose	Frequency	Pros	Cons	Notes
<b>Spironolactone Oral</b> (Aldactone)	100mg - 300mg (1-3x 100mg tablets)	400mg (4x 100mg tablets)	Daily	<ul style="list-style-type: none"> <li>Inexpensive</li> <li>Very effective to decrease endogenous testosterone levels</li> </ul>	<ul style="list-style-type: none"> <li>Potential risk of hyperkalemia</li> <li>Diuretic effect can result in fatigue, dehydration side effects</li> <li>Erectile dysfunction<sup>8</sup></li> </ul>	<ul style="list-style-type: none"> <li>Single or divided doses dependent on preference</li> </ul>
<b>Finasteride Oral</b> (Propecia or Proscar) As adjuvant anti-androgen	5mg (1x 5mg tablet)	5mg (1x 5mg tablet)	Daily	<ul style="list-style-type: none"> <li>Slows and prevents balding due to androgenic alopecia and decreases other secondary sexual hair growth in youth</li> </ul>		<ul style="list-style-type: none"> <li>Used as adjuvant because decreases DHT but not Testosterone</li> <li>Can use alone (without estrogen) if goal is only for partial feminization</li> </ul>
<b>Dutasteride Oral</b> (Avodart) As adjuvant anti-androgen	0.5mg (1x 0.5mg tablet)	0.5mg (1x 0.5mg tablet)	Every 3 days	<ul style="list-style-type: none"> <li>Slows and prevents balding due to androgenic alopecia and decreases other secondary sexual hair growth in youth</li> <li>Can take every 3 days rather than every day with Finasteride</li> </ul>	<ul style="list-style-type: none"> <li>May be expensive and not typically covered by insurance</li> </ul>	<ul style="list-style-type: none"> <li>Same as Finasteride Notes</li> </ul>
<b>Leuprolide Acetate IM</b> (Lupron, Eligard)	11.25mg (1 IM shot of 1.25mg/1.5mL dilutant)	22.5mg (2 IM shots of 11.25mg/1.5mL dilutant)	Every 3 months	<ul style="list-style-type: none"> <li>GnRH receptor agonist, very effective</li> <li>For Teens: Best option for puberty suppression; can use either alone or with exogenous hormones</li> <li>For Adults: Especially beneficial if can't use spiro and/or on a lower estrogen dose and/or having difficulty suppressing endogenous hormone production</li> </ul>	<ul style="list-style-type: none"> <li>May be expensive if not covered by insurance</li> <li>Not ideal for long-term use due to bone density loss<sup>5</sup></li> </ul>	
<b>Histrelin Pellet</b> (Vantas)	50mg	50mg	Every 1 year	<ul style="list-style-type: none"> <li>See Leuprolide Acetate Pros</li> </ul>	<ul style="list-style-type: none"> <li>More invasive, requires minor surgery to implant</li> <li>May be expensive if not covered by insurance</li> <li>Not ideal for long-term use due to bone density loss<sup>5</sup></li> </ul>	
Less Frequently Used Anti-Androgens	Start/Usual Dose	Typical Max Dose	Frequency	Pros	Cons	Notes
<b>Cyproterone Acetate Oral</b> (Androcur)	50mg (1x 50mg)	100mg (2x 50mg tablets)	Daily	<ul style="list-style-type: none"> <li>Steroidal androgen receptor antagonist, blocks T &amp; DHT very effectively</li> <li>Also a progestin agonist</li> </ul>	<ul style="list-style-type: none"> <li>Risk of meningioma; however, adverse effects are unlikely if using 100mg or less daily dose.</li> </ul>	<ul style="list-style-type: none"> <li>Unavailable in the US</li> </ul>
<b>Flutamide Oral</b> (Eulexin)	250mg (2x 125mg tablets)	250mg (2x 125mg tablets)	Daily	<ul style="list-style-type: none"> <li>Non-steroidal androgen receptor antagonist</li> </ul>	<ul style="list-style-type: none"> <li>Potential risk of rapid onset, severe, life-threatening liver toxicity; use extreme caution and monitor closely</li> <li>Don't use if +G6PD, or increased risk of methemoglobinemia (e.g. smokers); caution if other hepatotoxic drugs or alcohol.</li> </ul>	<ul style="list-style-type: none"> <li>If utilized must check LFT at baseline, 1 mo, 2 mo, then every 6 mo for lifetime</li> </ul>
<b>Bicalutamide Oral</b> (Casodex)	50mg (1x 50mg tablet)	50mg (1x 50mg tablet)	Daily	<ul style="list-style-type: none"> <li>Non-steroidal androgen receptor antagonist</li> </ul>	<ul style="list-style-type: none"> <li>See Flutamide Cons; however, Bicalutamide has less hepatotoxicity, so if choosing between non-steroidal androgen antagonists, choose Bicalutamide over Flutamide.</li> </ul>	<ul style="list-style-type: none"> <li>If utilized must check LFT at baseline, 1 mo, 2 mo, then every 6 mo for lifetime</li> </ul>

<sup>8</sup> If pt would like to experience erections with endogenous testosterone suppression and does not want to decrease anti-androgen dose, consider prescription of Viagra, Cialis, or if s/p orchiectomy can consider using low dose testosterone or Estratest

# Gender Affirming Hormone Therapy Guidelines

# TRANSLINE

Supplementary Medication	Start/Usual	Typical Max Dose	Frequency	Pros	Cons	Notes
<b>Micronized Progesterone Oral</b> (Prometrium)	100mg - 200mg (1x 100mg or 1x 200mg tablet)	200mg (1x 200mg tablet daily)	Daily	<ul style="list-style-type: none"> <li>Breast shape, mood, sex drive, weight gain. Weak evidence shows areola size may increase, but no evidence that it increases breast size—It may increase weight gain with a side effect of fuller breasts.</li> </ul>	<ul style="list-style-type: none"> <li>May increase risk of breast cancer additionally over estrogen use alone. With personal history of breast cancer, or known BRCA-mutation carrier, consider not prescribing. Avoid using cyclically due to higher risk of breast cancer compared to daily use.</li> </ul>	<ul style="list-style-type: none"> <li>Research is low quality to advise for or against; for those with a strong desire to try, a limited Rx is reasonable (e.g. 6 months). Engage in shared clinical decision-making about risks and benefits. Consider separate informed consent form or well documented consent.</li> </ul>
<b>Medroxyprogesterone Oral</b> (Provera)	2.5mg - 10mg (1x 2.5mg, 1x 5mg, or 1x 10mg tablet)	10mg (1x 10mg tablet daily)	Daily	<ul style="list-style-type: none"> <li>Same as Prometrium</li> </ul>	<ul style="list-style-type: none"> <li>Same as Prometrium</li> </ul>	<ul style="list-style-type: none"> <li>Only use if Prometrium is cost-prohibitive</li> </ul>
<b>Esterified Estrogen/Methyltestosterone Oral</b> (Estratest, Covaryx)	0.625mg/1.25mg	1.25mg/2.5mg	Daily	<ul style="list-style-type: none"> <li>Increased feeling of wellness and alleviation of fatigue associated with lack of androgen.</li> <li>Return of mild libido and interest in/return to intimate relationships</li> </ul>	<ul style="list-style-type: none"> <li>Same risks as those associated with estrogen</li> <li>Controlled substance</li> </ul>	<ul style="list-style-type: none"> <li>Dose of main source of estrogen should be adjusted to accommodate the increase included in the combo tablet. Generally, this is not a concern as most use Estratest after orchiectomy so they're less likely to require higher doses of estrogen for feminization.</li> </ul>

## Trans Feminine: Exogenous Estrogen Monitoring

This is in addition to any PCP visits or lab work indicated to monitor other health risks, disease states or standard medical screening.

Baseline	6-8 weeks after Initiation	After change in dose (6-8 weeks)	6 months after achieving maintenance dose (OPTIONAL, esp if otherwise young and healthy)	q12 months on stable maintenance dose (unless other concerns)	When to draw estrogen/prolactin?
BMP* Prolactin (only if on meds known to increase prolactin)	Testosterone (total), Estrogen (total)	Testosterone (total), Estrogen (total)	Testosterone (total), Estrogen (total), Prolactin**	BMP*, Testosterone (total), Estrogen (total), Prolactin	Injectable: One week after injection <sup>9</sup>  Oral & Transdermal: Trough (don't take/apply on the day of the draw)
PCP exam & BP	PCP exam & BP	PCP exam & BP	PCP exam & BP	PCP exam & BP	

\*BMP most important while using Spironolactone; If using max or above max estrogen dosages, if using Estrace, Flutamide or Bicalutamide, or if other medications or risks for hepatotoxicity present, check CMP rather than BMP.

\*\*If using max or above max estrogen dosages or if using Premarin, prolactin should be checked more rigorously. Otherwise, it's more important to screen for symptoms of prolactinoma than to check a level.

### Estradiol Reference Range:

- Use cisgender female follicular/pre-ovulatory phase reference range. Reference ranges may vary depending on lab.
- The goal is to be around or below mid-normal range for a cisgender female, but also it depends on goals of the client. If the patient hasn't had an orchiectomy, and is otherwise healthy, it is reasonable to be above the cis-gender female range.
- If estrogen is supraphysiologic, before making major adjustments, review administration technique to ensure correct dosing and re-check level. If persistently supraphysiologic, decrease dose and re-check again.
- Keep in mind that prolactin is a better indicator of persistently elevated estrogen levels.

### Testosterone Reference Range: <50 - 75ng/dL is ideal

- For persistently high testosterone, can consider increasing the anti-androgen dose or changing to a different type of anti-androgen if that is in line with patient goals.

### Prolactin Reference Range: <20 is ideal

- 20-40ng/dL is acceptable especially if on other medications that increase prolactin, but should re-check one month after the first time it is over 20 and then every 6 months thereafter.
- 40-80ng/dL consider decreasing estrogen or other prolactin inducing drug dosages, re-check in two weeks, one month, and then every 2 months until level is <40. If on injectable, can consider changing to oral or transdermal to avoid high peak of estrogen associated with injectable, which has the biggest effect on prolactin levels.
- 80ng/dL or higher: consider stopping or holding estrogen and all prolactin inducing medications during work up, re-check in two weeks, and consider MRI to rule out pituitary adenoma if prolactin is not lowering, or for any level above 100. Can consider re-starting estrogen after work-up is complete. Evaluate symptoms: if accompanied with galactorrhea or vision changes due to mass effect, consider MRI and/or short-course Cabergoline prescription.

### CBC Reference Range:

- Use CBC reference range for cisgender women.

### Abnormal BMP/CMP

- Consider switching anti-androgen medication types.

<sup>9</sup> Level will be higher if on every 10 or 14 day dosing than on every 7 day dosing



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# Gender Affirming Hormone Therapy Guidelines

## Medical Pearls

- Always keep in mind that hormone therapy dosing depends on the patient's goals of gender transition. Please recognize that these guidelines are merely common practice parameters; it is reasonable to go outside the minimum and maximum recommendations in certain circumstances. With harm reduction in mind, we generally recommend to treat the person and their level of satisfaction over lab values with exceptions, of course, in the setting of contraindications. For those looking for minimal effects and/or for adolescents, use less than the "start/typical" dosages. For more specific hormone therapy guidelines in adolescents please refer to the Gender Joy, Callen-Lorde, Endocrine Society, or UCSF Guidelines.
- Besides patient preference, choose the mode of delivery based on co-morbidities and shared medical decision-making.
- Interval increases in dose can begin as early as one month, with a target of achieving reasonable patient-driven goals; however, there's no evidence that starting very low and tapering up to usual dose is necessarily beneficial. Outside of the context of complex medical/psychosocial issues, it is reasonable to start prescribing at the typical dose if patient goals support that rather than tapering up.
- In addition, there's no evidence that starting at max doses is better to achieve full effects sooner either, with the exception of stopping menses sooner for trans masculine individuals on testosterone. In the rare case that someone is above the typical maximum dose, closer monitoring clinically with lab work may be warranted. Due to the potential aromatization of testosterone to estrogen and vice versa, higher doses may actually have the reverse intended effect.
- If continuing prescriptions for someone transferring care or if someone presents with long-term "self-therapy", providing a prescription for continued therapy at current doses may be reasonable so lab values may be checked on their current regimen.
- We recommend an informed consent model of hormone prescribing in which effects and risks, as well as fertility preservation options are discussed prior to prescribing, as is done with any other medication.