Dosing Guide: Gender Affirming Hormone Therapy

For Transgender and Gender Diverse Adolescents

MENSTRUAL SUPPRESSION

Menstruation commonly begins at Tanner 4+. Menstrual suppression may be a goal for some TGD adolescents. Pubertal blockade can accomplish this, but side effects are common (e.g. hot flashes). Below are dosing options for patients who desire only menstrual suppression. This will NOT block other effects of puberty (e.g. breast development, body fat redistribution, terminal hair growth, etc.)

Baseline testing

Consider pregnancy test if relevant after taking a thorough history

Medication Options	Dosing	Common Side Effects
Combined estrogen-progestin oral contraceptive pills (OCP)	Oral pill daily continuously prescribed	Abnormal uterine bleeding (AUB) if missed doses
Norethindrone acetate	Oral pill daily 5 mg initially; increase to 10 mg if menstrual suppression insufficient	AUB if missed doses or not taken at the same time each day; not effective for contraception
Levonorgestrel IUD	Q3-8 year; requires gyn exam and insertion.	Amenorrhea possible
Etonogestrel implant	Q3 year; inserted in clinic (upper arm)	Higher rates of AUB
Depo medroxy-progesterone acetate	Q3 month IM injection, clinic-administered	Weight gain, lower bone density

LABORATORY TESTING

No routine monitoring needed.

Next steps

Depending on patient preference. If switching to masculinizing hormone therapy, amenorrhea most often occurs after 3-6 months on low-dose testosterone. Increasing T dose may help achieve amenorrhea.

Download this Dosing Guide at:

https://bit.ly/TGD_dosing

Additional Resources:

For Tanner 5 dosing, see https://bit.ly/GAHT-QUICK-GUIDE.

Abbreviations: TGD = Transgender and Gender Diverse. GAHT = Gender Affirming Hormone Therapy. AMAB = assigned male at birth. AFAB = assigned female at birth. AUB = Abnormal Uterine Bleeding. T = testosterone. E = estradiol

References:

Endocrine Society Clinical Practice Guideline, 2017. (**https://bit.ly/EndoSoc2017**)

Seattle Children's Gender Clinic GAH Protocols. (**https://bit.ly/SeattleProtocol**)

WPATH SOC for the Health of TGD People, v8. (**https://bit.ly/WPATH_v8**)

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NOT A STANDALONE RESOURCE. Diagnostic criteria & approach to care are in the Visit Guide: https://bit.ly/TGD_visit . *Consider mental health referral for comprehensive biopsychosocial assessment & co-mgmt.*

Visit Guide at:

PUBERTY BLOCKADE

AFAB: Latest start is 2 years post-menarche (hot flashes possible if >1 yr post-menarche). Consider menstrual suppression if pubertal changes appear complete.
AMAB: Can start as late as Tanner 5 if preferred over androgen blocker.

Baseline testing	
Vitals (q3-6m)	Height, weight, sitting height, BP
Physical exam (q3-6m)	Tanner staging
Laboratory *best before 9am esp. in early puberty*	LH *(at baseline use ultrasensitive aka "pediatric" LH; level >0.3 mIU/mL = puberty starting)* FSH, estradiol, total T (via LC/MS)[1], vit D 25OH
Bone density (q6-12m)	DEXA of axial spine, femoral neck and hip at same facility (for comparison over time)
EKG (q1-2 yrs)	If FH of long QT or sudden cardiac death[2]
Starting dose	
Leuprolide (or other GnRH agonist)	IM (aka Lupron): 11.25 mg q3m SubQ (aka Eligard): 22.5 mg q3m, or 45 mg q6m
Histrelin (Supprelin)	50 mg subq implant q12-18 months

LABORATORY TESTING: *LH, FSH, estradiol, total testosterone, vit D 25OH*

Leuprolide: check above labs at 6 weeks (if 3-month version) or at 3 months (if 6-month version). Goal LH < 1, FSH < 4.3, estradiol < 20, total testosterone < 30
Histrelin: check above labs at 1 month after placement, then q6m for monitoring. Goal LH < 1, FSH <4.3, estradiol < 20, testosterone < 30

Dose adjustments

Consider increasing the dose if there is pubertal progression and labs show puberty is not suppressed (aka if labs are not in target ranges above)

Common side effects

Headache, fatigue, insomnia, muscle aches. Changes in weight, mood, breast tissue. AFAB: irregular period/spotting (if periods not suppressed). AMAB: inhibits spermatogenesis. Long term: low bone density, delayed growth plate closure

Next steps (after starting GAHT)

AFAB: Can dc when testosterone level >100 and/or on testosterone for >3-6 months. Some continue blockers until Testosterone is at adult levels (400-700).
AMAB: Estradiol may not suppress testosterone completely. When estradiol is at adult levels (>100), can consider either continuing puberty blockers or transitioning to spironolactone.
For ALL: DEXAs into adulthood (until 25-30 yo or until peak bone mass is reached)

[1] To measure low levels of testosterone LC/MS is the most appropriate testing method (immunoassay is not accurate at lower levels). [2] Reference: https://bit.ly/GNRH_QT

Induction of Puberty

For Transgender and Gender Diverse Adolescents

INDUCTION OF PUBERTY

Puberty blockade alone may be continued for several years before induction of puberty. To determine when to initiate puberty induction, WPATH SOC8 recommends an individualized approach based on comprehensive biopsychosocial assessment, rather than a strictly age-based approach.

MASCULINIZING (AFAB)

- For younger patients (<15 yo), masculinizing changes and testosterone levels should increase Q6 months over the course of 1-2 years to mimic puberty.
- Older patients can increase more quickly as desired (e.g. q3m)

Baseline testing

Total testosterone, estradiol, CBC; Urine HCG (if at risk for pregnancy); AST/ALT, lipid panel, A1c (if risk factors, family history, etc)

Medication	Pubertal induction protocol Start with the lowest dose below and increase every 6 months to the next dose.[3]	Post-pubertal adolescents Dose can be increased more rapidly, as below.
INJECTABLE TESTOSTERONE (T cypionate or T enanthate)	25 mg/m^2 q2wk (or ½ dose qwk) 50 mg/m^2 q2wk (or ½ dose qwk) 75 mg/m^2 q2wk (or ½ dose qwk) 100 mg/m^2/q2wk (or ½ dose qwk) Adult dose = 100-200 mg q2wk	75 mg q2wk for 6 months 125 mg q2wk Max adult dose 200 mg q2wk

LABORATORY TESTING. 1-3 months after starting, then q6 months
Check standard total testosterone, estradiol, CBC

- Injections: Labs checked at midpoint between injections
- Gel: at least 2 hours after application

Common side effects

Acne, androgenic hair loss, mood swings, emotional changes, increased libido, OSA, dyslipidemia, teratogenic (need for contraception), fertility effects not fully known, erythrocytosis (goal HCT <50%)
- If HCT 50-54%, hydrate and repeat labs 1-3 months
- If HCT >54%, start therapeutic phlebotomy and decrease dose or switch route/frequency. (i.e. change q2week injections to qweek instead)

needles: 18G 1 ½" to draw up &
1 mL 25G 5/8" to inject (subQ) OR
3 mL 23G 1-1.5" to inject (IM)

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FEMINIZING (AMAB)

- If on GnRH agonist for puberty blockade, may continue this **and** add feminizing hormones. Alternate: Androgen blocker may be substituted for GnRH agonist.
- For younger patients (<15 yo): feminizing changes and estradiol levels should increase Q6 months over the course of 1-2 years to mimic puberty.
- Older patients may increase more quickly as desired (e.g. q3m)

Baseline testing

Estradiol, total testosterone; potassium, BUN, creatinine (if using spironolactone); lipid panel, A1c (if risk factors, family history, etc.)

Starting dose

Medication	Pubertal induction protocol Start with the lowest dose below and increase every 6 months to the next level.[3]	Post-pubertal adolescents Dose can be increased more rapidly, as below.
ORAL ESTRADIOL	5 ug/kg/d 10 ug/kg/d 15 ug/kg/d 20 ug/kg/d Adult dose = 2-6 mg/d	1 mg/day for 6 months 2 mg/day Max adult dose 6 mg.
TRANSDERMAL ESTRADIOL	6.25-12.5 ug/24h 25 ug/24h 37.5 ug/24h Adult dose = 50-200 ug/24h	Notes about patches: - patches applied q3-4d - smallest patch is 25 ug; for lowest doses, apply ¼ or ½. Only cut matrix patches.
+ ANTI-ANDROGEN *At induction doses, E alone may not be sufficient to block T*	Leuprolide 11.25 mg subq q3m (or alt GnRH agonist)	No dose adjustments
	Spironolactone 25 mg bid	Titrate by 25 mg bid q3-6m. Typical: 100-300 mg/day. Max dose 400 mg/day.
ORAL PROGESTERONE	100-200 mg PO qhs.	Consider after using estradiol for ≥6m (if pts interested)

LABORATORY TESTING. 1-3 months after starting, then Q6m
Check E, total T, K, BUN, creatinine (if using spironolactone)

- Patch: Draw at least 24 h after application
- Oral: Draw at least 4 h after dose

Potential side effects

Estradiol: VTE, breast cancer, cholelithiasis, ? effect on fertility.
Spiro: Hyper-K, polyuria, low BP, decreased sperm motility.
Progesterone: Mood changes, acne

[3]Dose adjustments should be tailored based to individual patient goals. For example, nonbinary patients may benefit from lower doses. Make dose adjustments based on (1) lab results, (2) Tanner staging, (3) patient experience/goals.