

## Gender Dysphoria Hormone Therapy

### Policy Number: C8840-A

**CRITERIA EFFECTIVE DATES:**

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
09/01/2019	7/31/2019	7/31/2020
J CODE	TYPE OF CRITERIA	LAST P&T APPROVAL/VERSION
	RxPA	Q3 2019 20190828C8840-A

**\*\*\*THE INTENTION OF THIS CRITERIA IS TO REVIEW AND APPROVE APPROPRIATE USES OF HORMONAL THERAPY FOR THE PURPOSE ON NON-SURGICAL TREATMENT OF GENDER DYSPHORIA. ALL OTHER INDICATIONS FOR USE OF THESE HORMONAL PRODUCTS ARE ADDRESSED IN OTHER UTILIZATION MANAGEMENT CRITERIA\*\*\***

**PLEASE COORDINATE WITH HEALTHCARE SERVICES ANY NEED FOR SURGERY APPROVAL/DENIAL CONFIRMATION- { InterQual 2018.2 CP: Procedures: Specialized Procedures: Gender Reassignment Surgery}**

**PRODUCTS AFFECTED:**

Androgens: Androderm (testosterone transdermal patch), Androgel (testosterone topical gel), Delatestryl (testosterone enanthate), Depo-Testosterone (testosterone cypionate), Testopel (testosterone pellet for implant)  
Estrogens: Alora (estradiol transdermal patch), Delestrogen (estradiol valerate), Depo-Estradiol (estradiol cypionate), Estrace (estradiol oral tablet), Minivelle (estradiol transdermal patch) Vivelle (estradiol transdermal patch), Vivelle-Dot (estradiol transdermal patch)  
Gonadotropin-Releasing Hormone Agonist: Lupron Depot (leuprolide), Lupron Depot-Ped (leuprolide), Eligard (Leuprolide Acetate), Lupaneta Pack (Leuprolide & Norethindrone Tab Kit), Supprelin LA (histrelin acetate implant), Vantas (histrelin acetate implant)  
5-Alpha Reductase Inhibitor: Propecia tablets (finasteride)  
Aldosterone Receptor Antagonist: Aldactone (spironolactone)  
Progestin: Depo-Provera (medroxyprogesterone acetate), Progesterone

**DRUG CLASS:**

Androgens, Estrogens, Antineoplastic Agent, Gonadotropin-Releasing Hormone Agonist, 5-Alpha Reductase Inhibitor, Progestins

**ROUTE OF ADMINISTRATION:**

Injectable (intramuscular, subcutaneous), topical, oral

**PLACE OF SERVICE:**

Retail Pharmacy, Specialty Pharmacy, Buy and Bill- **MUST USE J9217 FOR ONCOLOGY INDICATIONS, MUST USE J1950 FOR WOMEN'S HEALTH AND CPP INDICATIONS**

**AVAILABLE DOSAGE FORMS:**

Androderm transdermal patch 2mg, 4mg, AndroGel packet 1.62% (1.25g, 2.5g), gel pump 1.62%, Delatestryl (enanthate) injectable solution 200mg/mL, Depo-Testosterone (cypionate) injectable solution 100mg/mL, 200mg/mL, Testopel pellet for implantation 75mg, Alora transdermal patch 0.025mg, 0.05mg, 0.075mg, 0.1mg, Delesrogen (valerate) injectable solution 10mg/mL, 20mg/mL, 40mg/mL, Depo-estradiol (cypionate) injectable solution 5mg/mL, Estrace oral tablet 0.5mg, 1mg, 2mg, Minivelle/Vivelle/Vivelle-Dot transdermal patch 0.025mg, 0.0375mg, 0.05mg, 0.075mg, 0.1mg,

Eligard 7.5 mg SC every 1 month, 22.5 mg SC every 3 months, 30 mg SC every 4 months, 45 mg SC every 6 months, Lupaneta Pack (11.25 mg IM for 3 months Norethindrone acetate 5 mg tablets), Lupron Depot 3.75 mg (monthly), 7.5 mg (monthly), Lupron Depot 11.25 mg (3 months), 22.5 mg (3 month), Lupron Depot 30 mg (4 months), Lupron Depot 45 mg (6 months), Lupron Depot-Ped (monthly) 7.5 mg, 11.25 mg, 15 mg, Lupron Depot -Ped (3 month) 11.25 mg, 30 mg, Supprelin LA implant 50mg, Vantas Implant 50mg, Finasteride oral tablets 1mg, Aldactone (spironolactone) oral tablets 25mg, 50mg, 100mg, Depo-Provera (medroxyprogesterone acetate) suspension for injection 150mg/mL, Progesterone oral capsules 100mg, Progesterone oil for injection 50mg/ml

**FDA-APPROVED USES:**

Androgens: Primary or Hypogonadotropic Hypogonadism (congenital or acquired), Delayed Puberty, Metastatic Breast Cancer

Estrogens: Menopause, Metastatic Breast Cancer, Hypogonadism, Post-menopausal osteoporosis, Advanced Androgen-Dependent Prostate Cancer (for palliation)

Gonadotropin-Releasing Hormone Agonist: Advanced prostate cancer, Endometriosis and Uterine leiomyomata fibroids, Central precocious puberty

5-Alpha Reductase Inhibitor: Benign prostatic hyperplasia, alopecia

Aldosterone Receptor Antagonist: Edema, Heart failure, Hyperaldosteronism, Hypertension

Progestin: Contraception, Endometriosis, Endometrial carcinoma/hyperplasia, Renal cell carcinoma, Secondary Physiologic amenorrhea

**COMPENDIAL APPROVED OFF-LABELED USES:**

For all products: Gender dysphoria (Transgender Health), Puberty suppression

5-Alpha Reductase Inhibitor: Hirsutism

Aldosterone Receptor Antagonist: Acute vulgaris, Chronic lung disease, Hirsutism, Polycystic ovary syndrome, Premenstrual Syndrome, Pulmonary Edema

Progestin: Andropause, Hot flashes, Hyperparathyroidism, Menopause, Paraphilia

Gonadotropin-Releasing Hormone Agonist: Ovarian cancer, Breast cancer

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**COVERAGE CRITERIA: INITIAL AUTHORIZATION**

**DIAGNOSIS:** Gender Dysphoria, Delayed Puberty

**ALL OTHER DIAGNOSIS MUST USE ALTERNATIVE CRITERIA**

[Hypogonadism, Delayed Puberty, Advanced prostate cancer, Endometriosis, Anemia prior to uterine fibroid surgery, Precocious puberty, Premenopausal ovarian suppression in women with breast cancer, Treatment of paraphilia/hypersexuality, Premenstrual dysphoric disorder, Ovarian cancer]

**REQUIRED MEDICAL INFORMATION:****A. PUBERTY SUPPRESSION**

1. Documentation that the adolescent has started puberty (Tanner stage  $\geq$  G2/B2)  
AND
2. Less than 16 years of age  
AND
3. A definitive diagnosis of persistent gender dysphoria has been made and documented by a qualified mental health professional such as a licensed psychiatrist, psychologist or psychotherapist and all of the following are present: [ALL]
  - i. The adolescent has demonstrated a long lasting and intense pattern of gender dysphoria  
AND
  - ii. Gender dysphoria worsened with the onset of puberty

AND

iii. The disorder is not a symptom of another mental disorder

AND

4. Recommendation for puberty suppression treatment has been made by an endocrinologist who has confirmed the diagnosis of persistent gender dysphoria by the qualified mental health professional

AND

5. Initial hormone therapy must be prescribed by an endocrinologist preceded by all of the following: [ALL]
  - i. Documentation that the individual has the capacity to make a fully informed decision and to consent for treatmentAND
  - ii. Documentation that the parents or caretakers or guardians have consented to the treatment and are involved in supporting the adolescent through the treatment process

AND

6. FOR SUPPRELIN LA REQUESTS: Documentation of a labeled contraindication to Vantas (histrelin implant)

*\*\*\* There is a lack of reliable evidence that any one brand of GnRH agonist is superior to other brands for medically necessary indications outlined in this policy. Vantas and Eligard are less costly therapeutic options that are utilized for pubertal suppression and gender dysphoria. Because other brands are more costly and are likely to produce equivalent therapeutic results, other brands of GnRH agonists may be considered not medically necessary unless the member has a contraindication or intolerance to the two of the less costly brands, or there are other medical reasons they cannot be used instead. \*\*\**

## B. GENDER DYSPHORIA

1. Age 16 years or older

AND

2. The individual has the capacity to make a fully informed decision and to consent for treatment

AND

3. A definitive diagnosis of persistent gender dysphoria has been made and documented by a qualified mental health professional such as a licensed psychiatrist, psychologist or psychotherapist and all of the following are present: [ALL]

- a. The desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatment

AND

- b. The transsexual identity has been present persistently for at least two years

AND

- c. The disorder is not a symptom of another mental disorder

AND

- d. The disorder causes clinically significant distress or impairment in social, occupational, or other important areas of functioning

AND

4. Recommendation for hormone replacement treatment has been made by an endocrinologist who has confirmed the diagnosis of persistent gender dysphoria by the qualified mental health professional

AND

5. Initial hormone therapy must be prescribed by an endocrinologist preceded by all of the following: [ALL]

- a. Documentation that the individual has lived as their new gender full-time for 3 months or more prior to the administration of hormones  
AND
- b. Documentation of continuous psychotherapy after the initial evaluation for a minimum of three months to identify any comorbid psychiatric diagnosis that may require treatment  
AND
6. Documentation that the individual has demonstrable knowledge of the risks and benefits of hormone replacement  
AND
7. LHRH agents are not covered following sex confirmation surgery

Note: All other FDA labeled indications for Estrogens, 5-Alpha Reductase Inhibitors, Aldosterone Receptor Antagonists, and Progestins are covered without Prior Authorization requirement

**DURATION OF APPROVAL:** Initial authorization: LHRH: 6 months or until time of sex confirmation surgery, Testosterone: 6 months, Continuation of therapy: 12 months

**QUANTITY:**

Androgens and Estrogens: Refer to “Hormone Treatment Recommendations” below for guideline recommended regimen dosing

Eligard 7.5 mg 1 injection 28 days  
Eligard 22.5 mg 1 injection 84 days  
Eligard 30 mg 1 injection 112 days  
Eligard 45 mg 1 injection 168 days  
Lupron Depot 1-month 3.75 mg 1 injection 28 days  
Lupron Depot 1-month 7.5 mg 1 injection 28 days  
Lupron Depot 3-month 11.25 mg 1 injection 84 days  
Lupron Depot 3-month 22.5 mg 1 injection 84 days  
Lupron Depot 4-months 30 mg 1 injection 112 days  
Lupron Depot 6-month 45mg 1 injection 168- days  
Lupron Depot-Ped 7.5 mg 1 injection 28 days  
Lupron Depot-Ped 11.25 mg 1 injection 28 days  
Lupron Depot-Ped 15 mg 1 injection 28 days  
Lupron Depot -Ped 3- month 11.25 mg 1 injection 84 days  
Lupron Depot-Ped 3-month 30 mg 1 injection 84 days

Propecia tablets (finasteride): 1mg tablet daily  
Aldactone (spironolactone): 100 – 300 mg daily

Depo-Provera (medroxyprogesterone acetate) 3-month 150mg IM injection 84 days  
Progesterone: 20 – 60mg daily

**PRESCRIBER REQUIREMENTS:**

PUBERTY SUPPRESSION and GENDER DYSPHORIA: Prescribed by or in consultation with an Endocrinologist and Mental Health Specialist (Refer to Required Medical Information)

**AGE RESTRICTIONS:**

PUBERTY SUPPRESSION: Tanner stage  $\geq$  G2/B2 through 16 years of age  
GENDER DYSPHORIA: 16 years of age or older

**GENDER:**

Male and female

**CONTINUATION OF THERAPY:****A. ALL INDICATIONS:**

1. Must submit documentation that member has been assessed by prescriber at least every 3 to 6 months for response to treatment, compliance, side effects (through regular monitoring of parameters such as height, weight, sitting height, Tanner stage, FH, FSH, estradiol/testosterone levels, renal/liver function, lipids, glucose, insulin, glycosylated hemoglobin, bone density, bone age, etc), and discussion of treatment plan (e.g. hormone therapy, sex confirmation surgery)

**CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:**

Patients with a FDA labeled contraindication to an individual agent are excluded from coverage unless the prescriber provides an attestation of medical necessity.

**BACKGROUND:**

Transsexualism also known as gender dysphoria is the condition in which a person with apparently normal somatic sexual differentiation of one gender is convinced that he or she is actually a member of the opposite gender. It is associated with an irresistible urge to be in the opposite gender hormonally, anatomically, and psychosocially. According to the American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders (DSM-V) gender dysphoria is described as a condition in which an individual is intensely uncomfortable with their biological gender and strongly identifies with, and wants to be, the opposite gender. For a person to be diagnosed with gender dysphoria there must be a marked difference between the individual's expressed/experienced gender and the gender others would assign him or her, and it must continue for at least six months. In children, the desire to be of the other gender must be present and verbalized. This condition causes clinically significant distress or impairment in social, occupational, or other important areas of functioning. Gender dysphoria is manifested in a variety of ways, including strong desires to be treated as the other gender or to be rid of one's sex characteristics, or a strong conviction that one has feelings and reactions typical of the other gender. It is recommended that patients meet the DSM-5 and/or ICD-10 criteria to be diagnosed with gender dysphoria. <sup>7</sup>

The current ICD-10 criteria for transsexualism include: <sup>10</sup>

The desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatments.

The transsexual identity has been present persistently for at least two years.

The disorder is not a symptom of another mental disorder or a genetic, intersex, or chromosomal abnormality.

The current DSM-5 criteria for gender dysphoria in adolescents and adults include: <sup>4,7</sup>

- A. Marked incongruence between one's experienced/expressed gender and natal gender of at least 6 months in duration, as manifested by at least two of the following:



- a. A marked incongruence between one's experienced/expressed gender and primary and or/ secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
  - b. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
  - c. A strong desire for the primary and/or secondary sex characteristics of the other gender
  - d. A strong desire to be of the other gender (or some alternative gender different from one's designated gender)
  - e. A strong desire to be treated as the other gender (or some alternative gender different from one's designated gender)
  - f. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's designated gender)
- B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:

1. The condition exists with a disorder of sex development
2. The condition is post transitional, in that the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or treatment regimen – namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (e.g., penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

The treatment of gender dysphoria requires a multidisciplinary team and step-wise approach to promote optimal health for individuals of this diverse population. The initial assessment of a patient with transsexualism is based on psycho-diagnostic instruments and ideally should be performed by a mental health professional who is trained in using the DSM-5 or ICD criteria. "Gender affirmation" or "transitioning" is defined as the process of reflection, acceptance, and intervention. Counseling is essential before initiating hormonal or surgical treatment for gender affirmation. It is recommended that when or before hormone treatment starts, the individual should begin living in the role of the opposite gender. The World Professional Association for Transgender Health Standards of Care provides the following criteria for starting hormone therapy and for undergoing surgical procedures: diagnosis of persistent, well-documented gender dysphoria, the capacity to make a well-informed decision, the person must be of legal age; and any medical or mental issues are well-controlled.

Medical management involves the suppression of puberty in the form of gonadotropin-releasing hormone agonists, followed by cross-sex hormone therapy to induce puberty by the age of 16. The two major goals of hormonal therapy are to reduce endogenous sex hormone levels and secondary sex characteristics of the individual's designated gender, and to replace endogenous sex hormone levels consistent with the individual's gender identity.<sup>7,10</sup>

Young adolescents with gender dysphoria may experience social distress due to pubertal changes. Gonadotropin-suppression or GnRH analogs are a reversible treatment option for adolescents with gender dysphoria which can be used up until the age of 16 to suppress puberty. It is suggested that pubertal hormone suppression should be started after girls or boys first exhibit physical changes of

puberty during Tanner stages G2/B2 (See Appendix A). This option provides time for the individual to explore gender identity and treatment options before gender-affirming sex hormone treatments and/or surgery. Studies reveal that pubertal suppression in children with gender dysphoria tends to lead to improved psychological function in adolescence and early adulthood. Regardless, pubertal suppression may be associated with long-term side effects including but not limited to bone mineralization. Therefore, individuals and providers should weigh the risks and benefits before initiating pubertal suppression in adolescents.<sup>7</sup>

Hormone replacement can begin at or after the age of 16 years. The goal of treatment in female-to-male transsexual individuals is to stop menses and induce virilization, including a male pattern of sexual hair, male physical contours, and clitoral enlargement. The principal hormonal treatment is a testosterone preparation. For male-to-female transsexual individuals the goal is elimination of sexual hair growth, induction of breast formation, and a more female fat distribution are essential. To accomplish this, a near-complete reduction of the biological effects of androgens is required.

### Puberty suppression treatment recommendations<sup>7, 12</sup>

- A. Treatment consists of IM injections of GnRH agonists:
  - a. Leuprolide 3.75 – 7 mg every month
  - b. Histrelin implant 50 µg/day released over a period of 12 months.
- B. The duration of treatment with GnRH agonists alone depends on when the individual reaches the age at which cross-sex hormone therapy can be added; typically, at the age of 16 years old

### Hormone treatment recommendations:<sup>7, 21</sup>

- A. There are different regimens to change secondary sex characteristics for transgender males. Parenteral, or transdermal preparations of testosterone can be used to achieve testosterone values in the normal male range, which is typically 320 to 1000 ng/dL. After the age of 40, transdermal formulations are recommended as they bypass first pass metabolism and seem to be associated with better metabolic profiles.

Testosterone for transgender males				
Parenteral		Transdermal		Implant
Testosterone enanthate	Testosterone cypionate	Testosterone gel 1.6%	Testosterone transdermal patch	Testopel®
100 – 200 mg/10 – 14 days or 50 – 100 mg/ week		50 – 100 mg/d	2.5 – 7.5 mg/d	75mg/pellet

- B. The hormone regimen for transgender females is more complex. While estrogens are the choice of therapy for transgender females, mono-therapy is typically not enough to reach testosterone levels in the female range (100 – 200 pg/mL and <50 ng/dL). Adjunctive anti-androgenic therapy may be necessary to achieve desirable androgen suppression. Transdermal preparations and injectable estradiol cypionate or valerate are advantageous in older transgender females who may be at higher risk for thromboembolic disease.

Estrogen for transgender females			
Oral	Transdermal	Parenteral	
Estradiol	Estradiol patch	Estradiol valerate	Estradiol cypionate

2 – 6 mg/d	0.025 – 0.2 mg/d *new patch placed Q3-5 d	5 – 30 mg IM Q2 weeks	2 – 10 mg IM Q week
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Anti-androgens for transgender females					
Progesterone	Medroxyprogesterone acetate	GnRH agonist (leuprolide)	Histrelin implant	Spironolactone	Finasteride
20 – 60 mg PO daily	150mg IM Q3 months	3.75 – 7.5mg IM monthly	50 mg implanted Q 12 months	100 – 300 mg PO daily	1 mg PO daily

### Surveillance recommendations:

#### For transgender men on Testosterone <sup>7</sup>

- Monitor for virilizing and adverse effects every 3 months for the first year, then every 6-12 months.
- Obtain baseline hematocrit and lipid profile and monitor every 3 months for the first year, then every 6 – 12 months.
  - Monitor weight, blood pressure, and lipids regularly during visits
- Obtain baseline bone mineral density if at risk for osteoporosis; routine screening after age 60, or earlier if sex hormone levels consistently low.
- Monitor serum estradiol during the first 6 months and thereafter until uterine bleeding has ceased.
- Monitor serum testosterone every 3 months until at , target levels, 320 – 1000 ng/dL
  - Peak levels for parenteral testosterone measured 24-48 hours after injection.
- Trough levels for parenteral measured before injection. If mastectomy was performed, conduct sub- and periareolar annual breast examinations.
  - If no mastectomy was performed, consider mammograms as recommended by the American Cancer Society

#### For transgender women on Estrogen <sup>7</sup>

- Monitor for feminizing and adverse effects every 3 months for the first year, then every 6-12 months.
- Obtain baseline hematocrit and lipid profile and monitor at follow up visits.
- Obtain baseline bone mineral density if at risk for osteoporosis; routine screening after age 60, or earlier if sex hormone levels consistently low.
- Obtain prolactin at baseline, at 12 months after initiation of treatment, biennially thereafter.
- Monitor serum testosterone every 3 months, target <50 ng/dL
- Monitor serum estradiol every 3 months, target 100-200 pg/mL .
- Obtain baseline serum potassium level and renal function, then every 3 months in the first year, and annually thereafter, when using Spironolactone.

### Other considerations:<sup>22-25</sup>

#### A. Breast cancer:

- FTM [female to male]: Intact breasts, routine screening as for natal females. Post-mastectomy: Yearly chest wall and axillary exams.



- ii) MTF [male to female]: Screening in patients >50 years with additional risk factors for breast cancer (estrogen therapy >5 years, family history, BMI >35).
- B. Cervical cancer:
  - i) FTM: Cervix intact, routine screening as for natal females.
- C. Prostate cancer:
  - i) MTF: Routine screening as for natal males.
- D. Cardiovascular disease:
  - i) Screen for risk factors.
- E. Diabetes mellitus:
  - i) MTF: Increased risk on estrogen.
  - ii) FTM: Routine screening.

## Summary of Medical Evidence<sup>8-12</sup>

There are no randomized controlled trials evaluating the effectiveness of hormone treatment for gender dysphoria. Available evidence consists of cross-sectional studies where a group of transgender individuals, some of whom had undergone cross-sex hormone therapy and some of whom had not, responded to questionnaires. Sample sizes in these studies of adults ranged from 50 to 376. The studies most commonly evaluated quality of life (QOL) or functional status with instruments such as the SF-36 Health Survey (QualityMetric Inc.), mood-related conditions such as depression or anxiety, and/or psychosocial conditions such as perceived social support or partnership status. A variety of other behavioral and social outcomes were each assessed, and results were generally positive.<sup>18-24</sup> A systematic review based on 28 studies (1833 participants; 1091 MtF and 801 FtM) published from 1996 to February 2008 included a meta-analysis of the QOL and psychosocial outcomes of hormone therapy. 80% of the study participants reported significant improvement in quality of life and reported significant improvement in psychiatric symptoms.<sup>25</sup>

Medically necessary criteria were developed according to the World Professional Association for Transgender Health Standards of Care, 7th version and the 2017 Endocrine Society clinical Practice Guidelines.<sup>4, 7</sup>

## APPENDIX:

### A. Tanner Stages of Breast Development and Male External Genitalia<sup>7</sup>

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**REFERENCES:**

1. Child Mind Institute. Gender Dysphoria Basics. Available at: <https://childmind.org/guide/guide-to-gender-dysphoria/treatment/>
2. Day P. Trans-gender reassignment surgery. New Zealand health technology assessment (NZHTA). The clearing house for health outcomes and Health technology assessment. February 2002; Volume 1 Number 1 Available at: [http://nzhta.chmeds.ac.nz/publications/trans\\_gender.pdf](http://nzhta.chmeds.ac.nz/publications/trans_gender.pdf).
3. World Professional Association for Transgender Health (WPATH). Standards of care for the health of transsexual, transgender, and gender nonconforming people. 7th version. 2011. Available at: [http://www.wpath.org/site\\_page.cfm?pk\\_association\\_webpage\\_menu=1351&pk\\_association\\_webpage=4655](http://www.wpath.org/site_page.cfm?pk_association_webpage_menu=1351&pk_association_webpage=4655)
4. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. 2013. Washington, DC. Pages 451-459.
5. American Psychiatric Association. Gender Dysphoria. 2013. Accessed at: <https://www.psychiatry.org/psychiatrists/practice/dsm/educational-resources/dsm-5-fact-sheets>
6. American Psychological Association. (2015). Guidelines for psychological practice with transgender and gender nonconforming people. *PsycEXTRA Dataset*, 70(9), 832-864. doi:10.1037/e527482015-001
7. Hembree WC, Cohen-Kettenis P, Gooren, Louis, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2017; 102(11):3869-3903.
8. World Health Organization (WHO). The ICD-10 Classification of Mental and Behavioural Disorders. 2016 Accessed at: <https://icd.who.int/browse10/2016/en#!/F64.0>
9. [Adelson SL; American Academy of Child and Adolescent Psychiatry \(AACAP\) Committee on Quality Issues \(CQI\). Practice parameter on gay, lesbian, or bisexual sexual orientation, gender nonconformity, and gender discordance in children and adolescents. J Am Acad Child Adolesc Psychiatry. 2012; 51\(9\):957-974.](#)
10. [American College of Obstetricians and Gynecologists \(ACOG\). The American College of Obstetricians and Gynecologists. Committee Opinion. Committee on Adolescent Health Care. Care for Transgender Adolescents. January 2017. Available at: https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Adolescent-Health-Care/Care-for-Transgender-Adolescents?IsMobileSet=false](#)
11. [Delemarre-van de Waal HA, Cohen-Kettenis PT. Clinical management of gender identity disorder in adolescents: a protocol on psychological and pediatric endocrinology aspects. European Journal of Endocrinology. 2006\(131-137\).](#)
12. Smith KP, Madison CM, Milne NM. Gonadal Suppressive and Cross-Sex Hormone Therapy for Gender Dysphoria in Adolescents and Adults. *American College of Clinical Pharmacy Journal*. 2014; 34(12):1282-1297

13. Heylens G., Verroken C., De Cock S., T'Sjoen G., De Cuypere G. Effects of different steps in gender reassignment therapy on psychopathology: a prospective study of persons with a gender identity disorder. *J Sex Med.* 2014;11(1):119-126.
14. Gorin-Lazard A, Baumstarck K, Boyer L, et al. Hormonal therapy is associated with better self-esteem, mood, and quality of life in transsexuals. *J Nerv Ment Dis.* 2013;201(11):996-1000.
15. Gorin-Lazard A, Baumstarck K, Boyer L, et al. Is hormonal therapy associated with better quality of life in transsexuals? A cross-sectional study. *J Sex Med.* 2012;9(2):531-541.
16. Colizzi M, Costa R, Todarello O. Transsexual patients' psychiatric comorbidity and positive effect of cross-sex hormonal treatment on mental health: Results from a longitudinal study. *Psychoneuroendocrinology.* 2014;39:65-73.
17. Fisher AD, Castellini G, Bandini E, et al. Cross-sex hormonal treatment and body uneasiness in individuals with gender dysphoria. *J Sex Med.* 2014;11(3):709-719
18. Costantino A, Cerpolini S, Alvisi S, Morselli PG, Venturoli S, Meriggiola MC. A prospective study on sexual function and mood in female-to-male transsexuals during testosterone administration and after sex reassignment surgery. *J Sex Marital Ther.* 2013;39(4):321-335.
19. Heylens G, Verroken C, De Cock S, T'Sjoen G, De Cuypere G. Effects of different steps in gender reassignment therapy on psychopathology: a prospective study of persons with a gender identity disorder. *J Sex Med.* 2014;11(1):119-126.
20. Wierckx K, Elaut E, Declercq E, et al. Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: a case-control study. *Eur J Endocrinol.* 2013;169(4):471-478.
21. Murad MH, Elamin MB, Garcia MZ, et al. Hormonal therapy and sex reassignment: a systematic review and meta-analysis of quality of life and psychosocial outcomes. *Clin Endocrinol (Oxf).* 2010;72(2):214-231.
22. Unger, Cecile A. Hormone therapy for transgender patients. *Transl Androl Urol.* 2016 Dec; 5(6): 877–884. doi: 10.21037/tau.2016.09.04
23. Hayes Medical Technology Directory. Hormone Therapy for the Treatment of Gender Dysphoria. Winifred Hayes Inc. Lansdale, PA. May 19, 2014. Updated April 18, 2017..
24. Hayes Medical Technology Directory. Ancillary Procedures and Services for the Treatment of Gender Dysphoria. Winifred Hayes Inc. Lansdale, PA. May 19, 2014. Updated April 18, 2017.
25. UpToDate: Tangpricha V. Safer J. Transgender women: Evaluation and management. Updated April 22, 2018.
26. UpToDate: Tangpricha V. Safer J. Transgender Men: Evaluation and management. Updated April 22, 2018.
27. UpToDate: Olson-Kennedy J, Forcier, M. Overview of the management of gender nonconformity in children and adolescents. 2017.
28. UpToDate: Olson-Kennedy J, Forcier, M. Management of transgender and gender-diverse children and adolescents, Updated April 2, 2019.

