



**INDIAN HEALTH SERVICE**  
**National Pharmacy and Therapeutics Committee**  
**Formulary Brief: Gender-Affirming Medications**  
**-February 2022-**



**Background:**

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a drug class review of gender-affirming medications at the Winter NPTC Meeting in February 2022. The evaluation included medications used in feminizing and masculinizing regimens and puberty suppression agents. Following clinical review and analysis of applicable guidelines and clinical evidence, the NPTC voted to (1) **ADD testosterone (any formulation)** and (2) **ADD estradiol (patch AND parenteral formulations)** to the National Core Formulary.

**Discussion:**

In the United States, 0.39% of the population identifies as transgender/gender non-conforming (TG/GNC).<sup>1</sup> Prevalence, or willingness to self-identify as transgender is increasing with prevalence doubling from 2011 to 2016 in a survey administered by The Williams Institute.<sup>2</sup> The prevalence is highest in those 18 to 24 years old and in non-white groups.<sup>2</sup>

The National Transgender Discrimination Survey reports higher rates of poorer socioeconomic outcomes such as living in extreme poverty (<\$10,000 per year), (15% TG/GNC vs. 4% US population) and homelessness (2% TG/GNC vs. 1% US population).<sup>3</sup> In this same survey, 63% of TG/GNC individuals reported experiencing at least one serious act of discrimination (such as losing a job, eviction, or assault) due to being transgender and 23% reported experiencing three or more such events<sup>3</sup>.

Lifetime suicide attempts are ten times greater in transgender people than in the general US population (41% vs. 4.6%) and are even higher in American Indian/Alaskan Native transgender people (56%).<sup>3</sup> The highest rate of lifetime suicide attempts is seen in transgender people who are refused medical treatment (60%).<sup>3</sup> Greater than 80% of all transgender people use, will use, or want hormone therapy through their life cycle<sup>3</sup>.

**Findings:**

The World Professional Association for Transgender Health publishes the [Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People](#), with Volume 7 most recently published in 2012 and Volume 8 anticipated in 2022.<sup>4</sup> These represent holistic international expert consensus guidelines for transgender healthcare. In the US, The Endocrine Society publishes the [Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons](#) clinical practice guidelines primarily focused on using medications in gender-affirming health care.<sup>5</sup> Together, these two guidelines form the starting point for treating transgender people in the US and inform many of the medico-legal dimensions of transgender healthcare such as insurance coverage.

The DSM-5 criteria for gender dysphoria are currently accepted as the diagnostic standard in the US for insurance coverage of gender-affirming hormone therapy or surgery. In addition to an individual experiencing incongruence between their experienced/expressed gender versus their assigned gender for at least six months, the incongruence must also result in clinically significant distress or impairment in social, occupational, or other important areas of functioning.<sup>6</sup> This diagnosis is distinct from gender incongruence defined by ICD-11 which requires “a strong desire to be treated as a person of the experienced gender” instead of distress or impairment.<sup>7</sup> Thus, it is important to note that an individual can be transgender—experiencing gender incongruence—without gender dysphoria.

Criteria for the use of hormone therapy for gender-affirmation in transgender people include: persistent, well-documented gender dysphoria, capacity (legal and otherwise) to provide informed consent, and medical and mental health concerns otherwise present must be reasonably well-controlled prior to starting hormone treatment. Provider responsibilities in initiating hormone therapy include evaluation and diagnosis and providing informed consent with discussion of the benefits and risks of gender-affirming medications—with particular attention to [fertility risk and fertility preservation options](#).<sup>6,8</sup>

All primary care providers should also ensure patients are offered appropriate preventive healthcare. In general, if an individual has a particular part or organ and otherwise meets criteria for screening, screening should proceed regardless of hormone use.<sup>8</sup> In those individuals no longer producing endogenous hormones and not taking cross-sex hormones, also consider osteoporosis screening.<sup>8</sup>

In general, the goals of gender-affirming hormone therapy are to suppress endogenous sex hormone levels, maintain sex hormones of a person’s affirmed gender in normal range for that gender, and monitor and manage side effects and risks of medications.<sup>7</sup>

For feminizing hormone therapy, estradiol (oral, transdermal, or parenteral form) promotes feminine body changes including redistribution of body fat, decreased muscle mass, and breast growth.<sup>7</sup> Dosing is dependent on the form used. Spironolactone is also commonly used at higher doses (50mg BID – 200mg BID) for antiandrogenic effects. Generally, testosterone levels should be <55 ng/dl and estradiol <200 pg/ml and monitored every three months in the first year and every 6-12 months thereafter.<sup>7</sup> If spironolactone is used, kidney function and potassium should also be monitored every 2-3 months in the first year, then at least annually thereafter.<sup>7</sup>

Estradiol is associated with a likely increased risk of venous thromboembolic disease, gallstones, elevated liver enzymes, and hypertriglyceridemia.<sup>6</sup> Also reported is a possible increased risk of cardiovascular disease, hypertension, hyperprolactinemia/prolactinoma, and type 2 diabetes.<sup>6</sup> An increased risk of breast cancer is inconclusive with current evidence.<sup>6</sup>

For masculinizing hormone therapy, testosterone (transdermal, parenteral) promotes masculine body changes including facial/body hair growth, scalp hair loss, fat redistribution, deepening of voice, clitoral enlargement, and vaginal atrophy.<sup>7</sup> Dosing is dependent on which form is used. Generally, testosterone levels should be in the normal physiological male range (300-1000 ng/dl) and are checked every three months in the first year and every 6-12 months thereafter.<sup>7</sup> Estradiol is also checked in the first six months (or until no uterine bleeding for six months) and should be <50 pg/ml.<sup>7</sup> Complete Blood Count and Liver Function Tests are monitored at baseline, every three months in the first year, and every 6-12 months thereafter.<sup>7</sup> The normal male physiologic range for hemoglobin/hematocrit should be used.

Testosterone is associated with a likely increased risk of polycythemia, acne, weight gain, androgenic alopecia, and sleep apnea.<sup>6</sup> Also reported is a possible increased risk of elevated liver enzymes, hyperlipidemia, cardiovascular disease, hypertension, and type 2 diabetes.<sup>6</sup> Evidence for loss of bone density, breast or cervical or uterine cancer is inconclusive with current evidence.<sup>6</sup>

#### **Conclusion:**

Use of hormone therapy for gender affirmation in transgender people experiencing gender dysphoria is an accepted international standard of care. Adding testosterone and estradiol to the National Core Formulary will help the IHS address the needs of a socially and medically vulnerable population of patients. With training and support (see below resources), initiation and maintenance of hormone therapy for transgender patients is appropriate in the primary care setting with the addition of these agents to the National Core Formulary.

#### **\*\*Additional Resources**

1. [Indian Country Trans & Gender Affirming Care ECHO Program](#)
2. [UCSF Transgender Care & Treatment Guidelines](#)
3. [VHA TRAIN](#)

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*If you have any questions regarding this document, please contact the NPTC at [IHSNPTC1@ihs.gov](mailto:IHSNPTC1@ihs.gov). For more information about the NPTC, please visit the [NPTC website](#).*

#### **References**

1. Meerwijk EL, Sevelius JM. [Transgender Population Size in the United States: a Meta-Regression of Population-Based Probability Samples](#). Am J Public Health. 2017 Feb;107(2): e1-e8.
2. Flores AR, Herman JL, Gates GJ, et al. [How Many Adults Identify as Transgender in the United States?](#) Los Angeles, CA: The Williams Institute, 2016
3. Grant JM, Mottet LA, Tanis J, et al. [Injustice at Every Turn: A Report of the National Transgender Discrimination Survey](#). Washington: National Center for Transgender Equality and National Gay and Lesbian Task Force, 2011.
4. World Professional Association for Transgender Health. [Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People](#) [7<sup>th</sup> Version]. 2012. Available online.
5. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. [Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline](#). J Clin Endocrinol Metab. 2017 Nov 1;102(11):3869-3903.
6. American Psychiatric Association. [Diagnostic and Statistical Manual of Mental Disorders](#). 5th ed. Arlington, VA: American Psychiatric Association Publishing.
7. World Health Organization (2021). [International statistical classification of diseases and related health problems](#) (11th ed.).
8. University of California San Francisco. UCSF Transgender Care, Department of Family and Community Medicine. [Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People](#); 2nd edition. Deutsch MB, ed. June 2016.