Testosterone Replacement or Supplementation Therapy (for Ohio Only)

Policy Number: CSOH2024D0076.B
Effective Date: June 1, 2024

Instructions for Use

Table of Contents **Page**

Related Policies
None

Application

This Medical Benefit Drug Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

Coverage Rationale

This policy refers to the following testosterone products:

- Testosterone cypionate (Depo-Testosterone®)
- Testosterone enanthate
- Testosterone pellets (Testopel®)
- Testosterone undecanoate (Aveed®)

Injectable testosterone and Testopel (testosterone pellets) are medically necessary for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone, including primary hypogonadism (congenital or acquired) and hypogonadotropic hypogonadism (congenital or acquired), when the following criteria are met:

- For **initial therapy**, **either** of the following:
  - Patient has history of **one** of the following:
    - Bilateral orchiectomy; **or**
    - Panhypopituitarism; **or**
    - A genetic disorder known to cause hypogonadism (e.g., congenital anorchia, Klinefelter's syndrome)

    or
  - **All** of the following:
    - **One** of the following:
      - Two pre-treatment early morning serum total testosterone levels less than 300 ng/dL (< 10.4 nmol/L) or less than the reference range for the lab, taken at separate times (this may require treatment to be temporarily held); **or**
      - **Both** of the following:
        - Patient has condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity); **and**

                - **One** pre-treatment calculated free or bioavailable testosterone level less than 50 pg/mL (< 5 ng/dL or < 0.17 nmol/L) or less than the reference range for the lab (this may require treatment to be temporarily held)

            and
        - Patient was male at birth; **and**
        - Diagnosis of hypogonadism; **and**
    - Dosing is in accordance with the U.S Food and Drug Administration (FDA) approved labeling; **and**
    - Initial authorization will be for no more than 6 months for new starts, 12 months for patients continuing therapy
- For **continuation of therapy**, **all** of the following:
    - **One** of the following:
        - Follow-up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e., on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e., on therapy for one year or longer), is **within** or below the normal male limits of the reporting lab; **or**
        - Follow up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e., on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e., on therapy for one year or longer), is **outside** of upper male limits of normal for the reporting lab and the dose is adjusted; **or**
        - **Both** of the following:
            - Patient has a condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity); **and**
            - **One** of the following:
                - Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e., on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e., on therapy for one year or longer), is **within** or below the normal male limits of the reporting lab; **or**
                - Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e., on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e., on therapy for one year or longer), is **outside** of upper male limits of normal for the reporting lab and the dose is adjusted

    and
    - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
    - Initial authorization will be for no more than 12 months

Injectable testosterone and Testopel (testosterone pellets) may be covered for gender-affirming hormonal therapy for transgender individuals when the following criteria are met:

- For **initial therapy**, **all** of the following:
    - Diagnosis of gender dysphoria, according to the current DSM (i.e., DSM-5-TR) criteria, by a mental health professional; **and**
    - Medication is prescribed by or in consultation with an endocrinologist or a medical provider knowledgeable in transgender hormone therapy; **and**
    - Authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
    - Diagnosis of gender dysphoria, according to the current DSM (i.e., DSM-5-TR) criteria, by a mental health professional; **and**
    - Medication is prescribed by or in consultation with an endocrinologist or a medical provider knowledgeable in transgender hormone therapy; **and**
    - **One** of the following:
        - Follow-up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e., on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e., on therapy for one year or longer), is **within** or below the normal male limits of the reporting lab; **or**
        - Follow up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e., on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e., on therapy for one year or longer), is **outside** of upper male limits of normal for the reporting lab and the dose is adjusted; **or**
        - **Both** of the following:
            - Patient has a condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity); **and**
            - **One** of the following:

- Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e., on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e., on therapy for one year or longer), is **within** or below the normal male limits of the reporting lab; **or**
- Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e., on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e., on therapy for one year or longer), is **outside** of upper male limits of normal for the reporting lab and the dose is adjusted

and

- Authorization will be for no more than 12 months

Compounded Hormone Products (e.g., Pellets)

Compounded drugs, including compounded testosterone, estrogen, or progesterone pellets are not FDA approved.[3] Compounded hormone products (e.g., pellets), including but not limited to compounded testosterone, estrogen, and progesterone pellets, are considered experimental and investigational and not covered for any indication.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
11980	Subcutaneous hormone pellet implantation

CPT® is a registered trademark of the American Medical Association

HCPCS Code	Description
J1071	Injection, testosterone cypionate, 1 mg
J3121	Injection, testosterone enanthate, 1 mg
J3145	Injection, testosterone undecanoate, 1 mg
S0189	Testosterone pellet, 75 mg

Diagnosis Code	Description
E23.0	Hypopituitarism
E23.3	Hypothalamic dysfunction, not elsewhere classified
E29.1	Testicular hypofunction
E30.0	Delayed puberty
E89.3	Postprocedural hypopituitarism
E89.5	Postprocedural testicular hypofunction
F64.0	Transsexualism
F64.1	Dual role transvestism
F64.2	Gender identity disorder of childhood
F64.8	Other gender identity disorders
F64.9	Gender identity disorder, unspecified
N44.00	Torsion of testis, unspecified
N45.2	Orchitis
Q53.00	Ectopic testis, unspecified
Q53.01	Ectopic testis, unilateral
Q53.02	Ectopic testes, bilateral
Q53.10	Unspecified undescended testicle, unilateral

Diagnosis Code	Description
Q53.111	Unilateral intraabdominal testis
Q53.112	Unilateral inguinal testis
Q53.12	Ectopic perineal testis, unilateral
Q53.20	Undescended testicle, unspecified, bilateral
Q53.211	Bilateral intraabdominal testes
Q53.212	Bilateral inguinal testes
Q53.22	Ectopic perineal testis, bilateral
Q53.9	Undescended testicle, unspecified
Q55.0	Absence and aplasia of testis
Z87.890	Personal history of sex reassignment
Z90.79	Acquired absence of other genital organ(s)

Maximum Dosage Requirements

Maximum Allowed Quantities by HCPCS Units

This section provides information about the maximum dosage for testosterone administered by a medical professional.

Medication Name		Maximum Dosage per Administration	HCPCS Code	Maximum Allowed
Brand	Generic			
Aveed	testosterone undecanoate	750 mg	J3145	750 HCPCs units (1 mg per unit)
N/A	testosterone enanthate	400 mg	J3121	400 HCPCs units (1 mg per unit)
Depo-Testosterone	testosterone cypionate	400 mg	J1071	400 HCPCs units (1 mg per unit)
Testopel	testosterone pellet	450 mg	S0189	6 HCPCs units (75 mg per unit)

Maximum Allowed Quantities by National Drug Code (NDC) Units

The allowed quantities in this section are calculated based upon both the maximum dosage information supplied within this policy as well as the process by which NDC claims are billed. This list may not be inclusive of all available NDCs for each drug product and is subject to change. Absence of a specific NDC does not mean that it is not subject to the following maximum allowed.

Medication Name		How Supplied	National Drug Code	Maximum Allowed
Brand	Generic			
Aveed	testosterone undecanoate	750 mg/3 mL	67979-0511-43	3 mL
N/A	testosterone enanthate	200 mg/mL	00574-0821-05 00143-9750-01 00591-3221-26	2 mL
Depo-Testosterone	testosterone cypionate	100 mg/mL	00009-0347-02 00009-0085-10 62756-0017-40 00409-6557-01 00781-3073-70	4 mL
Depo-Testosterone	testosterone cypionate	200 mg/mL	00517-1830-01 00143-9005-01 00781-3074-71 00781-3074-70 52536-0625-10 52536-0625-01	2 mL

Medication Name		How Supplied	National Drug Code	Maximum Allowed
Brand	Generic			
Depo-Testosterone	testosterone cypionate		64980-0467-99 69097-0802-32 69097-0802-37 00574-0827-01 76519-1210-00 00009-0086-01 00009-0417-01 50090-0330-00 00409-6562-02 00409-6562-22 00143-9659-01 62756-0016-40 00409-6562-01 00409-6562-20 76420-0650-01 00591-4128-79 00009-0086-10 00574-0827-10 62756-0015-40 00143-9726-01 00009-0417-02 63874-1061-01 00574-0820-01 00574-0820-10	
Testopel	testosterone pellet	75 mg pellet	66887-0004-01 66887-0004-10 66887-0004-20	6 pellets

Maximum Allowed Frequencies

The allowed frequencies in this section are based upon the FDA approved prescribing information for the applicable medications. For indications covered by UnitedHealthcare without FDA approved dosing, the frequencies are derived from available clinical evidence. This list may not be inclusive of all medications listed and is subject to change.

Medication Name		Maximum Frequency
Brand	Generic	
Aveed	testosterone undecanoate	The recommended dose is 750 mg initially, followed by 750 mg after 4 weeks, then 750 mg every 10 weeks thereafter.
N/A	testosterone enanthate	For replacement therapy, the suggested dosage is 50 mg to 400 mg every 2 to 4 weeks, not to exceed 400 mg per 14 days.
Depo-Testosterone	testosterone cypionate	For replacement in the hypogonadal male, the suggested dosage is 50 mg to 400 mg every 2 to 4 weeks, not to exceed 400 mg per 14 days.
Testopel	testosterone pellet	The dosage guideline for the testosterone pellets for replacement therapy in androgen-deficient males is 150 mg to 450 mg subcutaneously every 3 to 6 months. The usual dosage is as follows: implant two 75 mg pellets for each 25 mg testosterone propionate required weekly. Thus, when a patient requires injections of 75 mg per week, it is usually necessary to implant 450 mg (6 pellets). With injections of 50 mg per week, implantation of 300 mg (4 pellets) may suffice for approximately three months.

Background

Endogenous androgens are responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. These effects include the growth and maturation of prostate, seminal

vesicles, penis, and scrotum; the development of male hair distribution such as beard, pubic, chest and axillary hair, laryngeal enlargements, vocal cord thickening, alterations in body musculature and fat distribution.[1]

Clinical Evidence

In the 2018 update to the Testosterone Therapy in Men With Androgen Deficiency Syndromes guideline published in 2010, the authors recommend making a diagnosis of hypogonadism only in men with symptoms and signs consistent with testosterone (T) deficiency.[9] The group recommends fasting morning total T concentrations along with confirmation be used for monitoring. Measurement of free T concentration should be completed when total T is near the lower limit of normal or when a condition that alters sex hormone-binding globulin is present. Upon confirmation of androgen deficiency, the committee recommends additional diagnostic evaluation to determine the cause. T therapy is recommended for symptomatic men with T deficiency to induce and maintain secondary sex characteristics and correct symptoms of hypogonadism. Potential benefits and risks and benefits of T replacement should be discussed with the patient prior to initiating therapy. Upon initiation of T therapy, T concentration goals should be in the mid-normal range during treatment with any of the approved formulations, taking into consideration patient preference, pharmacokinetics, formulation-specific adverse effects, treatment burden, and cost. Men receiving T therapy should be monitored to evaluate symptoms, adverse effects, and compliance; measuring serum T and hematocrit concentrations; and evaluate prostate cancer risk after initiating T therapy.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Androgens are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired): Testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testes syndrome; or orchiectomy
- Hypogonadotropic hypogonadism (congenital or acquired): Gonadotropic (luteinizing hormone-releasing hormone) LHRH deficiency, or pituitary - hypothalamic injury from tumors, trauma or radiation

Safety and efficacy of Testopel (testosterone pellets) in men with age-related hypogonadism, also referred to as late-onset hypogonadism, have not been established[1, 13]. The dosage guideline for the testosterone pellets for replacement therapy in androgen-deficient males is 150 mg to 450 mg subcutaneously every 3 to 6 months. The usual dosage is as follows: implant two 75 mg pellets for each 25 mg testosterone propionate required weekly. Thus, when a patient requires injections of 75 mg per week, it is usually necessary to implant 450 mg (6 pellets). With injections of 50 mg per week, implantation of 300 mg (4 pellets) may suffice for approximately three months.

Aveed (testosterone undecanoate injection) is administered 750 mg initially, at week 4, then every 10 weeks thereafter.

Testosterone cypionate and testosterone enanthate injections are administered 50 mg to 400 mg every 2 to 4 weeks, not to exceed 400 mg per 14 days.

Compounded testosterone, estrogen, and progesterone pellets are not currently FDA approved and there has not been an FDA submission for approval of these products.

References

1. Testopel [prescribing information]. Malvern, PA: Endo Pharmaceuticals, Inc.; August 2018.
2. Seftel A. Testosterone replacement therapy for male hypogonadism: Part III. Pharmacologic and clinical profiles, monitoring, safety issues, and potential future agents. Int J Impot Res. 2007;19(1):2-24.
3. FDA Compounding Laws and Policies. https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm606881.htm. Accessed October 27, 2023.
4. Mulhall JP, et al. Evaluation and Management of Testosterone Deficiency: AUA Guideline. American Urological Association Education and Research, Inc 2018.
5. U.S. Food and Drug Administration (FDA). Testosterone Products: Drug Safety Communication. https://www.fda.gov/Drugs/DrugSafety/ucm436259.htm. Accessed October 27, 2023.

6. The World Professional Association for Transgender Health (WPATH), Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People, 7th Version.
7. Bhasin, S, et al. Testosterone replacement and resistance exercise in HIV-infected men with weight loss and low testosterone levels. *JAMA*. 2000. 283.(6) 763-770.
8. 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; 102:3869.
9. The Endocrine Society. Testosterone therapy in Adult Men with Androgen Deficiency Syndromes. J Clin Endocrinol Metab, May 2018, 103(5):1–30.
10. Depo-testosterone [prescribing information]. New York, NY: Pharmacia & Upjohn Co.; August 2018.
11. Aveed [prescribing information]. Malvern, PA: Endo Pharmaceuticals; August 2021.
12. Coleman E, Radix AE, Bouman WP, et al. Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. Int J Transgend Health. 2022;23(Suppl 1):S1-S259. Published 2022 Sep 6. doi:10.1080/26895269.2022.2100644.
13. Qaseem A, Horwitch CA, Vijan S, et al. Testosterone Treatment in Adult Men With Age-Related Low Testosterone: A Clinical Guideline From the American College of Physicians. Ann Intern Med. 2020;172(2):126-133. doi:10.7326/M19-0882.

Policy History/Revision Information

Date	Summary of Changes
06/01/2024	**Coverage Rationale** • Revised coverage criteria: ***Replacement Therapy in Conditions Associated with a Deficiency or Absence of Endogenous Testosterone*** ○ Removed criterion requiring: ▪ The patient is not taking any of the following: – Growth hormones, unless diagnosed with panhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Norditropin NordiFlex, Nutropin, Nutropin AQ, Omnitrope, Saizen, Zomacton – Aromatase inhibitor [e.g., Arimidex (anastrozole), Femara (letrozole), Aromasin (exemestane)] ▪ One of the following: – Significant reduction in weight (< 90% ideal body weight) (e.g., AIDS wasting syndrome) – Osteopenia – Osteoporosis – Decreased bone density – Decreased libido – Organic cause of testosterone deficiency (e.g., injury, tumor, infection, or genetic defects) ▪ Replaced criterion requiring: – "Panhypopituitarism *(defined as two or more pituitary hormone insufficiencies prior to the diagnosis of hypogonadism)*" with "panhypopituitarism" – "Two pre-treatment early morning serum total testosterone levels less than 300 ng/dL (< 10.4 nmol/L) or less than the reference range for the lab, taken at separate times (this may require treatment to be temporarily held) *(document lab value and date for both levels)*" with "two pre-treatment early morning serum total testosterone levels less than 300 ng/dL (< 10.4 nmol/L) or less than the reference range for the lab, taken at separate times (this may require treatment to be temporarily held)" ***Gender-Affirming Hormonal Therapy for Transgender Adults*** ○ Removed criterion requiring the patient is not taking any of the following growth hormones, unless diagnosed with panyhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Norditropin NordiFlex, Nutropin, Nutropin AQ, Omnitrope, Saizen, or Zomacton **Supporting Information** • Archived previous policy version CSOH2023D0076.A

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state (Ohio Administrative Code [OAC]), or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state (OAC), or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state (OAC), or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state (OAC), or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.