Testosterone Replacement or Supplementation Therapy

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Instructions for Use

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Related Policies
None

Applicable States

This Medical Benefit Drug Policy only applies to the states of Arizona, Maryland, North Carolina, Oklahoma, Tennessee, Virginia, and Washington.

Coverage Rationale

See Benefit Considerations

This policy refers to the following testosterone products:

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

Injectable testosterone and Testopel (testosterone pellets) are proven 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).

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, one of the following:
  - Patient has history of one of the following:
    - Bilateral orchiectomy; or
    - Panhypopituitarism (defined as two or more pituitary hormone insufficiencies prior to the diagnosis of hypogonadism); 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) (document lab value and date for both levels); 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 is not taking any of the following:
    - Growth hormones, unless diagnosed with panhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Norditropin NordiFlex, Nutropin, Nutropin AQ, Omnitrope, Saizen, Tev-Tropin; and
    - Aromatase inhibitor (e.g., Arimidex [anastrozole], Femara [letrozole], Aromasin [exemestane])

    and
  - Patient was male at birth; and
  - Diagnosis of hypogonadism; and
  - One of the following:
    - Significant reduction in weight (< 90% ideal body weight) (e.g., AIDS wasting syndrome); or
    - Osteopenia; or
    - Osteoporosis; or
    - Decreased bone density; or
    - Decreased libido; or
    - Organic cause of testosterone deficiency (e.g., injury, tumor, infection, or genetic defects)

  and
- Dosing is in accordance with the United States Food and Drug Administration 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
  - 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, Tev-Tropin; and
        - Aromatase inhibitor (e.g., Arimidex [anastrozole], Femara [letrozole], Aromasin [exemestane])

      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 adults 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) 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
    - Patient is not taking any of the following any of the following growth hormones, unless diagnosed with panyhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Norditropin NordiFlex, Nutropin, Nutropin AQ, Omnitrope, Saizen, or Tev-Tropin; 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) 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
    - 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 Tev-Tropin; and
    - Authorization will be for no more than 12 months.

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

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 the member specific benefit plan document 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

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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
E30.0	Delayed puberty
F64.0	Transsexualism
N44.00	Torsion of testis, unspecified
Q53.00	Ectopic testis, unspecified
Q53.111	Unilateral intraabdominal testis
Q53.112	Unilateral inguinal testis
Q53.20	Undescended testicle, unspecified, bilateral
Q53.211	Bilateral intraabdominal testes
Q53.212	Bilateral inguinal testes
Q53.22	Ectopic perineal testis, bilateral
Q55.0	Absence and aplasia of testis
Z87.890	Personal history of sex reassignment
Z90.79	Acquired absence of other genital organ(s)
N45.2	Orchitis
Q53.01	Ectopic testis, unilateral
Q53.02	Ectopic testes, bilateral
Q53.9	Undescended testicle, unspecified
Q53.10	Unspecified undescended testicle, unilateral
Q53.12	Ectopic perineal testis, unilateral
F64.1	Dual role transvestism
F64.2	Gender identity disorder of childhood
F64.8	Other gender identity disorders
F64.9	Gender identity disorder, unspecified
E89.3	Postprocedural hypopituitarism
E89.5	Postprocedural testicular hypofunction
E29.1	Testicular hypofunction

Diagnosis Code	Description
E23.0	Hypopituitarism
E23.3	Hypothalamic dysfunction, not elsewhere classified

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	750mg	J3145	750 HCPCs units (1 mg per unit)
Delatestryl	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
Delatestryl	testosterone enanthate	200 mg/mL	00134-9750-01	2 mL
Depo-Testosterone	testosterone cypionate	200 mg/mL	00517-1830-01 52536-0625-10 52536-0625-01 64980-0467-99 69097-0802-32 69097-0802-37 00574-0827-01 76519-1210-00 00009-0086-01 00009-0417-01 00009-0520-01 69097-0536-37 69097-0537-31 69097-0537-37 50090-0330-00 00409-6562-02 00409-6562-22 00143-9659-01 62756-0017-40	2 mL

Medication Name		How Supplied	National Drug Code	Maximum Allowed
Brand	Generic			
			62756-0016-40 00409-6557-01 00409-6562-01 00409-6562-20 76420-0650-01 00591-4128-79 00009-0085-10 00009-0086-10 00574-0827-10 00009-0520-10 00009-0347-02 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 750mg initially, followed by 750mg after 4 weeks, then 750mg every 10 weeks thereafter.
Delatestryl	testosterone enanthate	For replacement therapy, 50 mg to 400 mg every 2 to 4 weeks, not to exceed 400 mg per month.
Depo-Testosterone	testosterone cypionate	For replacement in the hypogonadal male, 50 mg to 400 mg every 2 to 4 weeks, not to exceed 400 mg per month.
Testopel	testosterone pellet	The dosage guideline for the testosterone pellets for replacement therapy in androgen-deficient males is 150mg to 450mg subcutaneously every 3 to 6 months. The usual dosage is as follows: implant two 75mg pellets for each 25mg testosterone propionate required weekly. Thus when a patient requires injections of 75mg per week, it is usually necessary to implant 450mg (6 pellets). With injections of 50mg per week, implantation of 300mg (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]

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. See the Policy and Procedure addressing the treatment of serious rare diseases.

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 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. The dosage guideline for the testosterone pellets for replacement therapy in androgen-deficient males is 150mg to 450mg subcutaneously every 3 to 6 months. The usual dosage is as follows: implant two 75mg pellets for each 25mg testosterone propionate required weekly.Thus when a patient requires injections of 75mg per week, it is usually necessary to implant 450mg (6 pellets). With injections of 50mg per week, implantation of 300mg (4 pellets) may suffice for approximately three months.

Aveed (testosterone undecanoate injection) is administered 750mg 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 month.

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

Centers for Medicare and Medicaid Services (CMS)

Medicare does not have a National Coverage Determination (NCD) for testosterone pellets (Testopel®), testosterone cypionate (Depo-Testosterone®), testosterone enanthate (Delatestryl®) and testosterone undecanoate (Aveed®). Local Coverage Determinations (LCDs) exist for testosterone replacement therapy; see the LCD for Treatment of Males with Low Testosterone. Local Coverage Article (LCA) specific to testosterone pellets (Testopel®) exists; see the LCA for Testopel Coverage. LCAs do not exist for testosterone cypionate (Depo-Testosterone®), testosterone enanthate (Delatestryl®) and testosterone undecanoate (Aveed®).

Medicare may cover outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual, Chapter 15, §50 Drugs and Biologicals. (Accessed March 12, 2020)

References

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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 June 11, 2018.
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5. U.S. Food and Drug Administration (FDA). Testosterone Products: Drug Safety Communication. https://www.fda.gov/Drugs/DrugSafety/ucm436259.htm. Accessed June 8, 2018
6. The World Professional Association for Transgender Health (WPATH), Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People, 7th Version.
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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. Delatestryl [prescribing information]. Malvern, PA: Endo Pharmaceuticals Solutions, Inc.; October 2016.
11. Depo-testosterone [prescribing information]. New York, NY: Pharmacia & Upjohn Co.; August 2018.
12. Aveed [prescribing information]. Malvern, PA: Endo Pharmaceuticals; October 2019.

Policy History/Revision Information

Date	Summary of Changes
01/01/2021	• New Medical Benefit Drug Policy

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates.

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. 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.