

Testosterone Replacement or Supplementation Therapy

Policy Number: CS2021D0076E
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[Instructions for Use](#)

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| Commercial Policy |
| <ul style="list-style-type: none"> Testosterone Replacement or Supplementation Therapy |

Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

| State | Policy/Guideline |
|----------------|--|
| Indiana | None |
| Kansas | Refer to the state’s Medicaid clinical policy |
| Kentucky | Testosterone Replacement or Supplementation Therapy (for Kentucky Only) |
| Louisiana | Testosterone Replacement or Supplementation Therapy (for Louisiana Only) |
| North Carolina | None |
| Pennsylvania | Refer to the state’s Medicaid clinical policy |

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 (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, NutropinAQ, 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, NutropinAQ, 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)

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 |

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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 |
| 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 | 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 | 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 62756-0016-40 00409-6557-01 00409-6562-01 00409-6562-20 | 2 mL |

| | | | | |
|----------|---------------------|--------------|---|-----------|
| | | | 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 |
| 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 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

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 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.

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)/Local Coverage Articles (LCAs) exist; see the LCDs/LCAs for [Treatment of Males with Low Testosterone](#), [Testopel Coverage](#) and [Gender Reassignment Services for Gender Dysphoria](#).

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 October 2, 2020)

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 June 11, 2018.
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 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.
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; June 2020.

Policy History/Revision Information

| Date | Summary of Changes |
|------------|---|
| 08/01/2021 | <p>Application</p> <ul style="list-style-type: none"> Added language to indicate this policy does not apply to the states of Indiana and North Carolina |
| 02/01/2021 | <p>Application</p> <ul style="list-style-type: none"> Reformatted content Added language to indicate this policy does not apply to the state of Kentucky; refer to the state-specific policy version <p>Coverage Rationale</p> <ul style="list-style-type: none"> Removed reference to brand name “Delatestryl” (for testosterone enanthate) <p>Applicable Codes</p> <ul style="list-style-type: none"> Removed references to brand name “Delatestryl” (for testosterone enanthate) <p>Maximum Allowed Quantities by National Drug Code (NDC) Units</p> <ul style="list-style-type: none"> Updated list of applicable National Drug Codes (NDCs) for testosterone enanthate: <ul style="list-style-type: none"> Added 00143-9750-01, 00574-0821-05, and 00591-3221-26 Removed 00134-9750-01 <p>Maximum Allowed Frequencies</p> <ul style="list-style-type: none"> Changed maximum allowed frequency for: <ul style="list-style-type: none"> Testosterone enanthate from “for replacement therapy, 50 mg to 400 mg every 2 to 4 weeks, not to exceed 400 mg per <i>month</i>” to “for replacement therapy, <i>the suggested dosage is</i> 50 mg to 400 mg every 2 to 4 weeks, not to exceed 400 mg per <i>14 days</i>” Depo-Testosterone (testosterone cypionate) from “for replacement in the hypogonadal male, 50 mg to 400 mg every 2 to 4 weeks, not to exceed 400 mg per <i>month</i>” to “for replacement in the hypogonadal male, <i>the suggested dosage is</i> 50 mg to 400 mg every 2 to 4 weeks, not to exceed 400 mg per <i>14 days</i>” <p>Supporting Information</p> <ul style="list-style-type: none"> Updated <i>FDA</i>, <i>CMS</i>, and <i>References</i> sections to reflect the most current information Archived previous policy version CS2020D0076D |

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state 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 MCG™ Care Guidelines, 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.