COUPE HEALTH

PHARMACY UTILIZATION MANAGEMENT (UM) PROGRAM CRITERIA ACTIVITY

Provider Notification

Policies Effective: 4/3/2023 Notification Posted: 2/17/2023

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Revisions are effective the first of the month following a 45-day notification and comment period.

UM PROGRAM CRITERIA REVISED		
Testosterone Injection		
Program Type:	☒ Prior Authorization ☒ Quantity Limit ☒ Step Therapy	
Testosterone Injection	1. Updated total testosterone range to 300 to 1000 ng/dL 2. References added to support increase in upper normal limit 3. Updated dosing for all indications 4. Added update to contraindications (h/o of prostate CA)	

Prior Authorization Approval Criteria

Testosterone Injection

Generic name:	Testosterone injection
Brand name:	Aveed; Depo-Testosterone; Testone CIK; Xyosted
Medispan GPI:	T cypionate - 231000301020** T enanthate - 2310003020D5** MONY T undecanoate - 231000308020**
Medication class:	Androgen
FDA-approved uses:	**Male primary hypogonadism (congenital or acquired)** **Male hypogonadotropic hypogonadism (congenital or acquired)** **Gender Dysphoria**

Usual dose range:

Testosterone cypionate – adult males	Initial: 75-100mg IM once weekly OR 150-200mg every 2 weeks	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL
Testosterone enanthate – adult males	Initial: 75-100mg IM once weekly OR 150-200mg every 2 weeks	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL

Testosterone undecanoate – adult males ***Ultra long acting***	Initial: 750 mg IM as single dose.	Maintenance: 750 mg IM 4 weeks after initial dose, then 750 mg IM every 10 weeks thereafter; titrated to a total testosterone goal of 350 to 1000 ng/dL
Testosterone cypionate – gender dysphoria	Initial: IM: 100 to 200 mg every 2 weeks **or** 50 to 100 mg every week SQ: 50 to 100 mg every week	Maintenance: 50-100 mg every week or 200mg every other week (titrated to a total testosterone goal of 350 to 1000 ng/dL)
Testosterone enanthate - gender dysphoria	Initial: IM: 100 to 200 mg every 2 weeks **or** 50 to 100 mg every week SQ: 50 to 100 mg every week	Maintenance: 50-100 mg every week or 200mg every other week (titrated to a total testosterone goal of 350 to 1000 ng/dL)
Testosterone cypionate – pediatric males	25 to 400 mg IM every 2 to 4 weeks.	
Testosterone enanthate – pediatric males	25 to 400 mg IM every 2 to 4 weeks.	

Duration of Authorization:

Initial:	4 months
Ongoing:	12 months

Estimated Cost:

Criteria for use for adult male hypogonadism

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient is clinically diagnosed with hypogonadism confirmed by medical record documentation including lab documentation of morning serum testosterone concentrations below normal range (less than 350ng/dL)
- Patient has persistent signs and symptoms of androgen deficiency (pre-treatment):
    - Low libido, decreased morning erections, loss of body hair, low bone mineral density, gynecomastia, small testes, fatigue, depression, anemia, reduced muscle strength, increased fat mass
- Other reasons for androgen deficiency have been ruled out (e.g. adrenal insufficiency, hypopituitarism)
- Requests for Aveed, Depo-Testosterone, Testone CIK, Xyosted; patient has failure, contraindication, or intolerance to generic testosterone cypionate -AND- one topical generic testosterone (gel or patch) product.

Criteria for use for gender dysphoria

- Request is for testosterone cypionate or testosterone enanthate only
- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient must be diagnosed with gender dysphoria, as defined by the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM)
- Requests for Depo-Testosterone, Testone CIK, Xyosted; patient has failure, contraindication, or intolerance to generic testosterone cypionate -AND- one topical generic testosterone (gel or patch) product.
- Patient is not taking any of the following
    - One of the following growth hormones, unless diagnosed with panhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Nutropin AQ, Omnitrope, Saizen
    - Aromatase inhibitor (eg, Arimidex [anastrozole], Femara [letrozole], Aromasin [exemestane])

Criteria for use for pediatric males

- Request is for testosterone cypionate or testosterone enanthate only

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient must be diagnosed with hypogonadism (primary) or hypogonadism (hypogonadotropic) (adolescent males)
- For patients diagnosed with delayed puberty, authorization will be for a limited duration (4 to 6 months)
- Requests for Depo-Testosterone, Testone CIK, Xyosted; patient has failure, contraindication, or intolerance to generic testosterone cypionate.

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Chart notes evaluating the safety and efficacy from within the prior 12 months are required for reauthorization.
- Patient demonstrates adequate compliance as defined as an MPR >80%.
- Adult male - follow-up total serum testosterone level drawn within the past 4 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 set therapeutic goal of 350 to 1000 ng/dL
- Gender Dysphoria - follow-up total serum testosterone level drawn within the past 4 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 set therapeutic goal of 350 to 1000 ng/dL

Contraindications:

- History of hypersensitivity to any of the product ingredients.
- Patients with breast cancer (males)
- Patients with prostate cancer (known or suspected). Exception- s/p radical prostatectomy for cancer confined to the prostate and patient has been free of disease (undetectable PSA) for at least 2 years
- Pregnancy
- Patients who may become pregnant
- Patients with serious cardiac, hepatic, or renal disease (testosterone cypionate only)
- men with hypogonadal conditions that are not associated with structural or genetic etiologies (eg, age-related hypogonadism) (testosterone enanthate subcutaneous injection only).
- Documentation of allergenic cross-reactivity for androgens is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty.

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.

Special Considerations:

- Subcutaneous testosterone enanthate can increase blood pressure (BP). Increased BP has been reported with other testosterone products as well. Check BP prior to initiation of therapy, at approximately 6 weeks and periodically thereafter. Some patients may require initiation or adjustment of antihypertensive therapy.
- Serious pulmonary oil microembolism (POME) reactions and anaphylaxis have been reported with testosterone undecanoate injection. Reactions include anaphylaxis, chest pain, urge to cough, dizziness, dyspnea, throat tightening, and syncope; may be life threatening. Reactions may occur after any injection during the course of therapy, including the first dose. Patients must be monitored for 30 minutes after injection. Due to the risk of serious POME reactions, Aveed is only available through the Aveed REMS Program. To minimize risk of adverse reactions, inject deeply into gluteal muscle. Rare reports of reactions

involving urge to cough, coughing fits, and respiratory distress immediately after the intramuscular injection of testosterone enanthate (an oil-based depot preparation) have also been reported.

- May cause hypercalcemia in patients with prolonged immobilization or cancer.
- Prolonged use of high doses of androgens has been associated with serious hepatic effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, jaundice). Prolonged use of IM testosterone enanthate has been associated with multiple hepatic adenomas. Discontinue therapy if signs or symptoms of hepatic dysfunction such as jaundice develop.
- Use with caution in patients with diseases that may be exacerbated by fluid retention, including cardiac impairment; testosterone may cause fluid retention. Treatment of androgen deficiency syndromes is not recommended for patients with uncontrolled or poorly controlled heart failure.
- Long-term use (more than 10 years) of parenteral testosterone for male hypogonadism may increase the risk of breast cancer.
- May cause gynecomastia, which may persist in patients treated for hypogonadism.
- Venous thromboembolic events including deep vein thrombosis (DVT) and pulmonary embolism (PE) have been reported with testosterone products. Evaluate patients with symptoms of pain, edema, warmth, and erythema in the lower extremity for DVT and those with acute shortness of breath for PE. Discontinue testosterone if a venous thromboembolism is suspected. Use in hypogonadal men with thrombophilia is not recommended.
- May alter serum lipid profile; use caution with history of myocardial infarction or coronary artery disease.
- May increase the risk of prostate cancer. Withhold therapy pending urological evaluation in patients with palpable prostate nodule or induration, prostate-specific antigen (PSA) more than 4 ng/mL, or PSA more than 3 ng/mL in patients at high risk of prostate cancer.
- May potentiate sleep apnea in some patients especially those with risk factors (eg, obesity or chronic lung disease). Withhold initial treatment in patients with untreated obstructive sleep apnea.
- Androgens may worsen BPH; use in patients with severe lower urinary tract symptoms ([AUA]/IPSS greater than 19) is not recommended. Discontinue therapy if urethral obstruction develops in patients with BPH (use lower dose if restarted).
- Priapism or excessive sexual stimulation may occur; discontinue therapy if this occurs; if restarted, a lower dose should be used.
- May increase hematocrit requiring dose adjustment or discontinuation. Withhold initial treatment in patients with hematocrit greater than 48% or greater than 50% if living at higher altitudes. Discontinue therapy if hematocrit exceeds 54%; may reinitiate at lower dose.
- Testosterone therapy is indicated only for testosterone deficiency, NOT for impaired spermatogenesis. Testosterone therapy impairs spermatogenesis further by suppressing pituitary gonadotropin secretion.
- Use with caution in patients with depression; testosterone may increase risk of depression and suicidal ideation. Evaluate patients with new onset or worsening depression, anxiety, mood changes, or suicidal ideation or behavior.
- Some dosage forms may contain benzyl alcohol. Large amounts of benzyl alcohol (99 mg/kg/day or more) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; the "gasping syndrome" consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension, and cardiovascular collapse. Some data suggest that benzoate displaces bilirubin from protein-binding sites; avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling.
- Available studies are inconclusive regarding the risk of developing major adverse cardiovascular events (MACE) such as nonfatal myocardial infarction (MI), stroke, or cardiovascular death following testosterone use. Some studies have suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy, although the overall evidence does not demonstrate an increased or decreased cardiovascular risk. According to the FDA, prescribe testosterone therapy only for males with low testosterone levels caused by certain medical conditions (eg, disorders of the testicles, pituitary gland, or brain) and confirmed by laboratory tests. However, in a position statement issued by the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE), they recommend that after a thorough diagnostic work-up, testosterone replacement should be guided by signs and symptoms and

testosterone concentrations rather than the underlying cause. The Endocrine Society recommends avoiding testosterone therapy in men who have experienced an MI or stroke within the past 6 months. Evaluate patients for cardiovascular risk factors prior to initiating therapy and monitor closely during therapy for cardiovascular events.

References:

1. Depo-Testosterone (testosterone cypionate) [prescribing information]. New York, NY: Pfizer; August 2018.
2. Aveed (testosterone undecanoate) [prescribing information]. Malvern, PA: Endo Pharmaceuticals Inc; August 2021.
3. Testosterone. Lexi-Interact [database online]. Hudson, OH: Lexicomp Inc; 2015. http://online.lexi.com. Accessed April 20, 2015.
4. Testosterone. Lexi-Drugs [database online]. Hudson, OH: Lexicomp Inc; 2015. http://online.lexi.com. Accessed April 20, 2015.
5. Testosterone enanthate [prescribing information]. Eatontown, NJ: West-Ward Pharmaceuticals; November 2016.
6. Xyosted (testosterone) [prescribing information]. Ewing, NJ: Antares Pharma, Inc; September 2018.
7. . Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010;95(6):2536-2559.[PubMed 20525905]
8. Medras M, Filus A, Jozkow P, Winowski J, Sicinska-Werner T. Breast cancer and long-term hormonal treatment of male hypogonadism. Breast Cancer Res Treat
9. Centers for Disease Control and Prevention (CDC). Neonatal deaths associated with use of benzyl alcohol—United States. MMWR Morb Mortal Wkly Rep. 1982;31(22):290-291. http://www.cdc.gov/mmwr/preview/mmwrhtml/00001109.htm.[PubMed 6810084]
10. American Academy of Pediatrics Committee on Drugs. "Inactive" ingredients in pharmaceutical products: update (subject review). Pediatrics. 1997;99(2):268-278.[PubMed 9024461]
11. Harmonized Reference Ranges for Circulating Testosterone Levels in Men of Four Cohort Studies in the United States and Europe, *The Journal of Clinical Endocrinology & Metabolism*, Volume 102, Issue 4, 1 April 2017, Pages 1161–1173
12. Le M, Flores D, May D, Gourley E, Nangia AK. Current Practices of Measuring and Reference Range Reporting of Free and Total Testosterone in the United States. J Urol. 2016 May;195(5):1556-1561.
13. Testosterone replacement therapy following radical prostatectomy. J Sex Med. 2009;6(4):1165. Epub 2009 Jan 22.

MedOne Clinical Review Subcommittee approval: Date: 1-1-17

Initial adoption:	1-1-17
Revised:	10-8-22 2-8-23
10-8-22	1. Criteria updated to include Xyosted (testosterone enanthate)
2-8-2023	1. Updated total testosterone range to 300 to 1000 ng/dL 2. References added to support increase in upper normal limit 3. Updated dosing for all indications 4. Added update to contraindications (h/o of prostate CA)
Effective Date (most recent revisions):	4-3-23

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adopted this clinical policy and that is operated or administered, in whole or in part, by MedOne Pharmacy Benefits, or any of such health plan's affiliates, as applicable.

UM PROGRAM CRITERIA REVISED		
Testosterone Intranasal		
Program Type:	☒ Prior Authorization ☒ Quantity Limit	☒ Step Therapy
Testosterone Intranasal	1. Updated total testosterone range to 300 to 1000 ng/dL 2. References added to support increase in upper normal limit 3. Updated dosing for all indications 4. Added update to contraindications (h/o of prostate CA)	

Prior Authorization Approval Criteria

Testosterone Intranasal

Generic name: Testosterone intranasal
Brand name: Natesto
Medispan GPI: 23100030004080 MONY
Medication class: Androgen
FDA-approved uses: **Male primary hypogonadism (congenital or acquired)**
Male hypogonadotropic hypogonadism (congenital or acquired)

Usual dose range:

1% Gel – adult males	Initial: 11mg three times daily	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL

Duration of Authorization:
Initial: 4 months
Ongoing: 12 months

Estimated Cost:
~$4,200 per year

Criteria for use for adult male hypogonadism

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient is clinically diagnosed with hypogonadism confirmed by medical record documentation including lab documentation of morning serum testosterone concentrations below normal range (less than 300ng/dL)
- Patient has persistent signs and of androgen deficiency (pre-treatment):
  - Low libido, decreased morning erections, loss of body hair, low bone mineral density, gynecomastia, small testes, fatigue, depression, anemia, reduced muscle strength, increased fat mass
- Other reasons for androgen deficiency have been ruled out (e.g. adrenal insufficiency, hypopituitarism)
- For brand- Patient has failure, contraindication, or intolerance to at least TWO generic testosterone formulations- gel, patch, injection.

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.

- Chart notes evaluating the safety and efficacy from within the prior 12 months are required for reauthorization.
- Patient demonstrates adequate compliance as defined as an MPR >80%.
- Adult male - follow-up total serum testosterone level drawn within the past 4 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 set therapeutic goal of 350 to 1000 ng/dL

Contraindications:

- History of hypersensitivity to any of the product ingredients.
- Patients with breast cancer (males)
- Patients with prostate cancer (known or suspected). Exception- s/p radical prostatectomy for cancer confined to the prostate and patient has been free of disease (undetectable PSA) for at least 2 years
- Pregnancy
- Patients who may become pregnant
- Breastfeeding patients

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.

Special Considerations:

- Use is not recommended in patients with sinus disease, mucosal inflammatory disorders (eg, Sjogren syndrome), or with a history of nasal disorders, nasal or sinus surgery, nasal fracture within the previous 6 months, or nasal fracture that caused a deviated anterior nasal septum.
- Androgens may worsen benign prostatic hyperplasia (BPH); use in patients with severe lower urinary tract symptoms ([AUA]/IPSS >19) is not recommended. Discontinue therapy if urethral obstruction develops in patients with BPH (use lower dose if restarted)
- May increase the risk of prostate cancer.(Ref) Withhold therapy pending urological evaluation in patients with palpable prostate nodule or induration, prostate-specific antigen (PSA) more than 4 ng/mL, or PSA more than 3 ng/mL in patients at high risk of prostate cancer.
- May increase hematocrit requiring dose adjustment or discontinuation. Withhold initial treatment in patients with hematocrit >48% or >50% if living at higher altitudes. Discontinue therapy if hematocrit exceeds 54%; may reinitiate at lower dose.
- Testosterone therapy is indicated only for testosterone deficiency, NOT for impaired spermatogenesis. Testosterone therapy impairs spermatogenesis further by suppressing pituitary gonadotropin secretion.
- Venous thromboembolic events including deep vein thrombosis (DVT) and pulmonary embolism (PE) have been reported with testosterone products. Evaluate patients with symptoms of pain, edema, warmth, and erythema in the lower extremity for DVT and those with acute shortness of breath for PE. Discontinue therapy if a venous thromboembolism is suspected. Use in hypogonadal males with thrombophilia is not recommended.
- Safety and efficacy have not been established in males with a body mass index (BMI) greater than 35 kg/m2.
- Use with caution in patients with diseases that may be exacerbated by fluid retention including cardiac impairment; testosterone may cause fluid retention. Treatment of androgen deficiency syndromes is not recommended for men with uncontrolled or poorly controlled heart failure.
- May cause gynecomastia, which may persist in patients treated for hypogonadism.
- May potentiate sleep apnea in some patients, especially those with risk factors (eg, obesity or chronic lung disease). Withhold initial treatment in patients with untreated obstructive sleep apnea.
- May alter serum lipid profile; use caution with history of myocardial infarction (MI) or coronary artery disease.
- May cause hypercalcemia in patients with prolonged immobilization or cancer.

- Available studies are inconclusive regarding the risk of developing major adverse cardiovascular events (MACE) such as nonfatal myocardial infarction (MI), stroke, or cardiovascular death following testosterone use. Some studies have suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy, although the overall evidence does not demonstrate an increased or decreased cardiovascular risk. According to the FDA, prescribe testosterone therapy only for males with low testosterone levels caused by certain medical conditions (eg, disorders of the testicles, pituitary gland, or brain) and confirmed by laboratory tests. However, in a position statement issued by the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE), they recommend that after a thorough diagnostic work-up, testosterone replacement should be guided by signs and symptoms and testosterone concentrations rather than the underlying cause. The Endocrine Society recommends avoiding testosterone therapy in males who have experienced an MI or stroke within the past 6 months. Evaluate patients for cardiovascular risk factors prior to initiating therapy and monitor closely during therapy for cardiovascular events.

References:

1. Natesto (testosterone nasal gel) [prescribing information]. Englewood, CO: Aytu BioScience Inc; December 2017.
2. Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010;95(6):2536-2559.[PubMed 20525905]
3. Medras M, Filus A, Jozkow P, Winowski J, Sicinska-Werner T. Breast cancer and long-term hormonal treatment of male hypogonadism. Breast Cancer Res Treat
4. Centers for Disease Control and Prevention (CDC). Neonatal deaths associated with use of benzyl alcohol—United States. MMWR Morb Mortal Wkly Rep. 1982;31(22):290-291. http://www.cdc.gov/mmwr/preview/mmwrhtml/00001109.htm.[PubMed 6810084]
5. American Academy of Pediatrics Committee on Drugs. "Inactive" ingredients in pharmaceutical products: update (subject review). Pediatrics. 1997;99(2):268-278.[PubMed 9024461]
6. Harmonized Reference Ranges for Circulating Testosterone Levels in Men of Four Cohort Studies in the United States and Europe, *The Journal of Clinical Endocrinology & Metabolism*, Volume 102, Issue 4, 1 April 2017, Pages 1161–1173
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8. Testosterone replacement therapy following radical prostatectomy. J Sex Med. 2009;6(4):1165. Epub 2009 Jan 22.

MedOne Clinical Review Subcommittee approval: Date: 1-1-17

Initial adoption: 1-1-17

Revised: 2-8-23

2-8-2023

1. Updated total testosterone range to 300 to 1000 ng/dL
2. References added to support increase in upper normal limit
3. Updated dosing for all indications
4. Added update to contraindications (h/o of prostate CA)

Effective Date (most recent revisions): 4-3-23

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external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by MedOne Pharmacy Benefits, or any of such health plan's affiliates, as applicable.

UM PROGRAM CRITERIA REVISED		
Testosterone Oral		
Program Type:	☒ Prior Authorization ☒ Quantity Limit ☒ Step Therapy	
Testosterone Oral	1. Updated total testosterone range to 300 to 1000 ng/dL 2. References added to support increase in upper normal limit 3. Updated dosing for all indications 4. Added update to contraindications (h/o of prostate CA)	

Prior Authorization Approval Criteria

Testosterone Oral

Generic name: Testosterone oral
Brand name: Jatenzo
Medispan GPI: 231000308001** MONY
Medication class: Androgen
FDA-approved uses: **Male primary hypogonadism (congenital or acquired)**
Male hypogonadotropic hypogonadism (congenital or acquired)

Usual dose range:

Adult males	Initial: 237mg twice daily	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL

Duration of Authorization:
Initial: 4 months
Ongoing: 12 months

Estimated Cost:
~$7,000-14,000 per year

Criteria for use for adult male hypogonadism

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient is clinically diagnosed with hypogonadism confirmed by medical record documentation including lab documentation of morning serum testosterone concentrations below normal range (less than 300ng/dL)
- Patient has persistent signs and symptoms of androgen deficiency (pre-treatment):
  - Low libido, decreased morning erections, loss of body hair, low bone mineral density, gynecomastia, small testes, fatigue, depression, anemia, reduced muscle strength, increased fat mass
- Other reasons for androgen deficiency have been ruled out (e.g. adrenal insufficiency, hypopituitarism)
- Patient has failure, contraindication, or intolerance to two topical generic testosterone (gel or patch) products -OR- one topical product -AND- generic testosterone cypionate injection.
- For brand- patient has failure, contraindication, or intolerance to at least TWO generic testosterone formulations- gel, patch, injection.

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Chart notes evaluating the safety and efficacy from within the prior 12 months are required for reauthorization.
- Patient demonstrates adequate compliance as defined as an MPR >80%.
- Adult male - follow-up total serum testosterone level drawn within the past 4 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 set therapeutic goal of 350 to 1000 ng/dL

Contraindications:

- History of hypersensitivity to any of the product ingredients.
- Patients with breast cancer (males)
- Patients with prostate cancer (known or suspected). Exception- s/p radical prostatectomy for cancer confined to the prostate and patient has been free of disease (undetectable PSA) for at least 2 years
- Pregnancy
- Men with hypogonadal conditions that are not associated with structural or genetic etiologies (eg, age-related hypogonadism).

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.

Special Considerations:

- Increase in blood pressure has been observed with oral testosterone undecanoate. These effects have been reported with other testosterone products as well. Check blood pressure prior to initiation of therapy, at approximately 3 weeks and periodically thereafter. Some patients may require initiation or adjustment of antihypertensive therapy.
- May increase hematocrit requiring dose adjustment or discontinuation. Withhold initial treatment in patients with hematocrit >48% or >50% if living at higher altitudes. Discontinue therapy if hematocrit exceeds 54%; may reinitiate at lower dose.
- Testosterone therapy is indicated only for testosterone deficiency, NOT for impaired spermatogenesis. Testosterone therapy impairs spermatogenesis further by suppressing pituitary gonadotropin secretion.
- Available studies are inconclusive regarding the risk of developing major adverse cardiovascular events (MACE) such as nonfatal myocardial infarction (MI), stroke, or cardiovascular death following testosterone use. Some studies have suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy, although the overall evidence does not demonstrate an increased or decreased cardiovascular risk. According to the FDA, prescribe testosterone therapy only for males with low testosterone levels caused by certain medical conditions (eg, disorders of the testicles, pituitary gland, brain) and confirmed by laboratory tests. However, in a position statement issued by the American Association of Clinical Endocrinologists and the American College of Endocrinology, they recommend that after a thorough diagnostic work-up, testosterone replacement should be guided by signs and symptoms and testosterone concentrations rather than the underlying cause. The Endocrine Society recommends avoiding testosterone therapy in males who have experienced an MI or stroke within the past 6 months. Evaluate patients for cardiovascular risk factors prior to initiating therapy and monitor closely during therapy for cardiovascular events.
- Androgens may worsen benign prostatic hyperplasia (BPH); use in patients with severe lower urinary tract symptoms (American Urological Association/International Prostate Symptom Score >19) is not recommended. Discontinue therapy if urethral obstruction develops in patients with BPH (use lower dose if restarted).

- May increase the risk of prostate cancer. Withhold therapy pending urological evaluation in patients with palpable prostate nodule or induration, PSA >4 ng/mL, or PSA >3 ng/mL in patients at high risk of prostate cancer.
- Venous thromboembolic events, including DVT and PE, have been reported with testosterone products. Evaluate patients with symptoms of pain, edema, warmth, and erythema in the lower extremity for DVT and those with acute shortness of breath for PE. Discontinue therapy if a venous thromboembolism is suspected. Use in hypogonadal men with thrombophilia is not recommended.
- Prolonged use of high doses of androgens has been associated with serious hepatic effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, jaundice). Discontinue therapy if signs or symptoms of hepatic dysfunction (such as jaundice) develop.
- May cause gynecomastia, which may persist in patients treated for hypogonadism.
- May potentiate sleep apnea in some patients, especially those with risk factors (eg, obesity, chronic lung disease). Withhold initial treatment in patients with untreated obstructive sleep apnea.
- May alter serum lipid profile; use caution with history of MI or coronary artery disease.
- May cause hypercalcemia in patients with prolonged immobilization or cancer.
- Use with caution in patients with depression; testosterone may increase risk of depression and suicidal ideation. Evaluate patients with new onset or worsening depression, anxiety, mood changes, or suicidal ideation or behavior.
- Use with caution in patients with diseases that may be exacerbated by fluid retention, including cardiac impairment; testosterone may cause fluid retention. Treatment of androgen deficiency syndromes is not recommended for patients with uncontrolled or poorly controlled heart failure.

References:

9. Jatenzo (testosterone) oral [prescribing information]. Northbrook, IL: Clarus Therapeutics Inc; June 2019.
10. Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010;95(6):2536-2559.[PubMed 20525905]
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exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy has been developed by licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by MedOne Pharmacy Benefits, or any of such health plan's affiliates, as applicable.

UM PROGRAM CRITERIA REVISED		
Testosterone Topical		
Program Type:	☒ Prior Authorization ☒ Quantity Limit ☒ Step Therapy	
Testosterone Topical	1. Updated total testosterone range to 300 to 1000 ng/dL 2. References added to support increase in upper normal limit 3. Updated dosing for all indications 4. Added update to contraindications (h/o of prostate CA)	

Prior Authorization Approval Criteria

Testosterone Topical

Generic name: Testosterone topical

Brand name: Androderm; AndroGel; AndroGel Pump; EC-RX Testosterone; Fortesta; Testim; Vogelxo; Vogelxo Pump

Medispan GPI: Testosterone Gel – 231000300040**
Testosterone Patch – 231000300085** MONY

Medication class: Androgen

FDA-approved uses: **Male primary hypogonadism (congenital or acquired)**
Male hypogonadotropic hypogonadism (congenital or acquired)
Gender Dysphoria

Usual dose range:

1% Gel – adult males	Initial: 50mg/day	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL
1.62% Gel – adult males	Initial: 40.5mg/day	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL
Fortesta – adult males	Initial: 40mg/day	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL
Transdermal Solutions – adult male	Initial: 60mg/day	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL
1% or 1.62% Gel – gender dyspmophia	Initial: 50-100mg/day	Maintenance: titrated to a total testosterone goal of 300 to 1000 ng/dL

Duration of Authorization:

Initial: 4 months

Ongoing: 12 months

Estimated Cost:

~$5,000 per year (gel)
~ $4,500-9,000 per year (patch)

Criteria for use for adult male hypogonadism

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient is clinically diagnosed with hypogonadism confirmed by medical record documentation including lab documentation of morning serum testosterone concentrations below normal range (less than 300ng/dL)
- Patient has persistent signs and symptoms (pre-treatment):
    - Low libido, decreased morning erections, loss of body hair, low bone mineral density, gynecomastia, small testes, fatigue, depression, anemia, reduced muscle strength, increased fat mass
- Other reasons for androgen deficiency have been ruled out (e.g. adrenal insufficiency, hypopituitarism)
- For brand- patient has failure, contraindication, or intolerance to at least TWO generic testosterone formulations- gel, patch, injection.

Criteria for use for gender dysphoria

- Request is for 1% or 1.62% gel only
- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient must be diagnosed with gender dysphoria, as defined by the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM)
- Patient is not taking any of the following:
    - One of the following growth hormones, unless diagnosed with panhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Nutropin AQ, Omnitrope, Saizen
    - Aromatase inhibitor (eg, Arimidex [anastrozole], Femara [letrozole], Aromasin [exemestane])
- For brand- patient has failure, contraindication, or intolerance to at least TWO generic testosterone formulations- gel, patch, injection.

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Chart notes evaluating the safety and efficacy from within the prior 12 months are required for reauthorization.
- Patient demonstrates adequate compliance as defined as an MPR >80%.
- Adult male - follow-up total serum testosterone level drawn within the past 4 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 set therapeutic goal of 350 to 1000 ng/dL
- Gender Dysphoria - follow-up total serum testosterone level drawn within the past 4 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 set therapeutic goal of 350 to 1000 ng/dL

Contraindications:

- History of hypersensitivity to any of the product ingredients.
- Patients with breast cancer (males)
- Patients with prostate cancer (known or suspected). Exception- s/p radical prostatectomy for cancer confined to the prostate and patient has been free of disease (undetectable PSA) for at least 2 years
- Pregnancy

- Patients who may become pregnant

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.

Special Considerations:

- Topical testosterone products may have different doses, strengths, or application instructions that may result in different systemic exposure; these products are not interchangeable.
- Androgens may worsen benign prostatic hyperplasia (BPH); use in patients with severe lower urinary tract symptoms ([AUA]/ IPSS >19) is not recommended. Discontinue therapy if urethral obstruction develops in patients with BPH (use lower dose if restarted).
- May increase the risk of prostate cancer. Withhold therapy pending urological evaluation in patients with palpable prostate nodule or induration, prostate-specific antigen (PSA) more than 4 ng/mL, or PSA more than 3 ng/mL in patients at high risk of prostate cancer.
- Testosterone may be transferred to another person following skin-to-skin contact with the application site. Virilization in children has been reported following contact with unwashed or unclothed application sites of men using topical testosterone. Patients should strictly adhere to instructions for use in order to prevent secondary exposure. Children and women should avoid contact with application sites of men using topical products. Symptoms of virilization generally regress following removal of exposure; however, in some children, enlarged genitalia and bone age did not fully return to age appropriate normal. Signs of inappropriate virilization in women or children following secondary exposure to topical testosterone should be brought to the attention of a health care provider.
- May increase hematocrit requiring dose adjustment or discontinuation. Withhold initial treatment in patients with hematocrit >48% or >50% if living at higher altitudes. Discontinue therapy if hematocrit exceeds 54%; may reinitiate at lower dose.
- Testosterone therapy is indicated only for testosterone deficiency, NOT for impaired spermatogenesis. Testosterone therapy impairs spermatogenesis further by suppressing pituitary gonadotropin secretion.
- Use with caution in patients with depression; testosterone may increase risk of depression and suicidal ideation. Evaluate patients with new onset or worsening depression, anxiety, mood changes, or suicidal ideation or behavior.
- Venous thromboembolic events including deep vein thrombosis (DVT) and pulmonary embolism (PE) have been reported with testosterone products. Evaluate patients with symptoms of pain, edema, warmth, and erythema in the lower extremity for DVT and those with acute shortness of breath for PE. Discontinue testosterone if a venous thromboembolism is suspected. Use in hypogonadal males with thrombophilia is not recommended.
- Prolonged use of high doses of androgens has been associated with serious hepatic effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, jaundice). Discontinue therapy if signs or symptoms of hepatic dysfunction (such as jaundice) develop.
- Use with caution in patients with diseases that may be exacerbated by fluid retention, including cardiac impairment; testosterone may cause fluid retention. Treatment of androgen deficiency syndromes is not recommended for patients with uncontrolled or poorly controlled heart failure.
- May cause gynecomastia, which may persist in patients treated for hypogonadism.
- May potentiate sleep apnea in some patients, especially those with risk factors (eg, obesity or chronic lung disease). Withhold initial treatment in patients with untreated obstructive sleep apnea.
- May alter serum lipid profile; use caution with history of MI or coronary artery disease.
- May cause hypercalcemia in patients with prolonged immobilization or cancer.
- Safety and efficacy of transdermal solution in males with body mass index >35 kg/m2 has not been established.
- Available studies are inconclusive regarding the risk of developing major adverse cardiovascular events (MACE) such as non-fatal MI, stroke, or cardiovascular death following testosterone use. Some studies have

suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy, although the overall evidence does not demonstrate an increased or decreased cardiovascular risk. According to the FDA, prescribe testosterone therapy only for males with low testosterone levels caused by certain medical conditions (eg, disorders of the testicles, pituitary gland, or brain) and confirmed by laboratory tests. However, in a position statement issued by the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE), they recommend that after a thorough diagnostic work-up, testosterone replacement should be guided by signs and symptoms and testosterone concentrations rather than the underlying cause. The Endocrine Society recommends avoiding testosterone therapy in males who have experienced an MI or stroke within the past 6 months. Evaluate patients for cardiovascular risk factors prior to initiating therapy and monitor closely during therapy for cardiovascular events.

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Initial adoption:	1-1-17
Revised:	2-8-23
2-8-2023	1. Updated total testosterone range to 300 to 1000 ng/dL 2. References added to support increase in upper normal limit 3. Updated dosing for all indications 4. Added update to contraindications (h/o of prostate CA)
Effective Date (most recent revisions):	4-3-23

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Please note:
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