

## DRUG QUANTITY MANAGEMENT POLICY – PER RX

- POLICY:** Testosterone Products (Topical) Drug Quantity Management Policy – Per Rx
- Transdermal Patch**
- Androderm<sup>®</sup> (testosterone transdermal system [2 mg/day and 4 mg/day] – Allergan)
- Transdermal Gels**
- AndroGel<sup>®</sup> (testosterone 1% gel, 1.62% gel – AbbVie, generic)
  - Fortesta<sup>™</sup> (testosterone 2% gel – Endo, generic)
  - Testim<sup>®</sup> (testosterone 1% gel – Endo, generic)
  - Vogelxo<sup>™</sup> (testosterone 1% gel – Upsher-Smith, generic)
- Transdermal Solution**
- testosterone 2% solution (Axiron<sup>™</sup> – Lilly, generic only)
- Nasal Gel**
- Natesto<sup>™</sup> (testosterone nasal gel – Acerus)
- Oral Testosterone Products**
- Striant<sup>™</sup> (testosterone buccal system, mucoadhesive – Endo) [obsolete]

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### OVERVIEW

The topical testosterone replacement products are all indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.<sup>1-9</sup> The labels for the FDA-approved products define those patients and/or conditions for which use of testosterone replacement products is indicated:

- **Primary hypogonadism (congenital or acquired):** testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above normal.
- **Hypogonadotropic hypogonadism (congenital or acquired):** gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations, but have gonadotropins in the normal or low range.

The diagnosis of male hypogonadism is based on both signs/symptoms and low testosterone levels. By restoring normal levels of testosterone, the replacement regimens correct symptoms of hypogonadism, which can include malaise, loss of muscle strength, depressed mood, and decreased libido.<sup>10</sup>

### Guidelines

- **Hypogonadism:** Guidelines from the American Urological Association (2018) note that clinicians should use a total testosterone level below 300 ng/dL as a reasonable cutoff in support of the diagnosis of low testosterone.<sup>11</sup> A clinical diagnosis requires low testosterone levels (two separate levels, both conducted in the early morning) combined with signs and symptoms. The Endocrine Society guidelines on testosterone therapy in men with hypogonadism (2018) recommend diagnosing hypogonadism in men with symptoms and signs of testosterone deficiency and unequivocally and consistently low serum total testosterone and/or free testosterone concentrations (when indicated).<sup>12</sup>

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- **Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Female-To-Male (FTM) Gender Reassignment (i.e., Endocrinologic Masculinization):** A clinical practice guideline published by the Endocrine Society (2017) recommends that, prior to initiation of hormonal therapy, the treating endocrinologist should confirm the diagnostic criteria of gender dysphoria/gender incongruence and the criteria for the endocrine phase of gender transition.<sup>13</sup> The clinician should also evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment. Guidelines mention that clinicians can use either parenteral or transdermal preparations to achieve appropriate testosterone values. The recommended dose of a transdermal testosterone patch cited in the guideline is 2.5 mg to 7.5 mg/day; testosterone gel is recommended at a dose of 50 to 100 mg/day.

## Dosing

### *Androderm*

The recommended starting dose is one 4 mg/day patch (not two 2 mg/day patches) applied nightly for 24 hours (to deliver 4 mg of testosterone/day).<sup>1</sup> To ensure proper dosing, approximately 2 weeks after starting therapy, the early morning serum testosterone concentration should be measured following system application in the previous evening. Serum testosterone concentrations measured in the early morning outside the range of 400 ng/dL to 930 ng/dL require increasing the daily dose up to 6 mg (as one 4 mg/day and one 2 mg/day patch) or decreasing the daily dose to 2 mg (as one 2 mg/day patch).

### *AndroGel (generic)*

The recommended starting dose of AndroGel 1% is 50 mg of testosterone (two 25 mg packets or one 50 mg packet), applied topically once daily (QD) in the morning to the shoulders and upper arms and/or abdomen area (preferably at the same time every day).<sup>3</sup> To ensure proper dosing, serum testosterone concentrations should be measured. If the serum testosterone concentration is below the normal range, the daily AndroGel 1% dose may be increased from 50 mg to 75 mg and from 75 mg to 100 mg for adult males as instructed by the physician.

The recommended starting dose of AndroGel 1.62% is 40.5 mg of testosterone (two pump actuations or a single 40.5 mg packet) applied topically QD in the morning to the shoulders and upper arms.<sup>4</sup> The dose can be adjusted between a minimum of 20.25 mg of testosterone (one pump actuation or a single 20.25 mg packet) and a maximum of 81 mg of testosterone (four pump actuations or two 40.5 mg packets). To ensure proper dosing, the dose should be titrated based on the pre-dose morning serum testosterone concentration from a single blood draw at approximately 14 days and 28 days after starting treatment or following dose adjustment. Table 1 provides the number of pumps or packets needed to achieve the desired AndroGel 1.62% dose.

**Table 1. AndroGel 1.62% Dosing.<sup>4\*</sup>**

Total Dose of Testosterone	Total Pump Actuations	Total Packets
20.25 mg	1 pumps	1 x 20.25 mg packet
40.5 mg	2 pumps	1 x 40.5 mg packet
60.75 mg	3 pumps	1 x 20.25 mg packet + 1 x 40.5 mg packet
81 mg	4 pumps	2 x 40.5 mg packets

\*The total number of pump actuations or packets are for each dosage form separately, not a combined dose to achieve the total dose of testosterone.

### *Fortesta (generic)*

The recommended starting dose of Fortesta is 40 mg (four pump actuations) of testosterone applied QD to the thighs in the morning.<sup>7</sup> The dose can be adjusted between a minimum of 10 mg of testosterone and a maximum of 70 mg of testosterone (Table 2). To ensure proper dosing, the dose should be titrated based

on the serum testosterone concentration from a single blood draw 2 hours after applying Fortesta at approximately Day 14 and Day 35 after starting treatment or following dose adjustment.

**Table 2. Fortesta Dosing.<sup>7</sup>**

Total Dose of Testosterone	Total Pump Actuations
10 mg	1
20 mg	2
30 mg	3
40 mg	4
50 mg	5
60 mg	6
70 mg	7

*Testim (generic)*

The recommended starting dose of Testim is 50 mg of testosterone applied QD to the shoulders and/or upper arms in the morning.<sup>2</sup> To ensure proper dosing, serum testosterone concentrations should be measured. Morning, pre-dose serum testosterone concentrations should be measured approximately 14 days after initiation of therapy to ensure proper serum testosterone concentrations are achieved. The daily Testim dose may be increased from 50 mg testosterone (1 tube) to 100 mg testosterone (2 tubes) QD. The maximum recommended dose is 100 mg QD.

*Vogelxo (generic)*

The recommended starting dose of Vogelxo is 50 mg of testosterone (one tube, one packet, or four pump actuations) applied QD to the shoulders and/or upper arms in the morning.<sup>8</sup> To ensure proper dosing, serum testosterone concentrations should be measured. Morning, pre-dose serum testosterone concentrations should be measured approximately 14 days after initiation of therapy to ensure proper serum testosterone concentrations are achieved. The daily Vogelxo dose may be increased from 50 mg of testosterone QD to 100 mg testosterone QD (two tubes, two packets, or eight pump actuations). The maximum recommended dose is 100 mg of testosterone QD.

*Natesto*

The recommended starting dose of Natesto is 11 mg of testosterone (two pump actuations; one actuation per nostril) administered intranasally three times daily for a total daily dose of 33 mg (6 pump actuations/day).<sup>9</sup> To ensure proper dosing, serum testosterone concentrations should be measured.

*Testosterone 2% topical solution (Axiron, generic only)*

The recommended starting dose of testosterone 2% topical solution is 60 mg of testosterone (two pump or two twist actuations) applied QD.<sup>6</sup> To ensure proper dosing, serum testosterone concentrations should be measured after initiation of therapy to ensure that the desired concentrations (300 ng/dL to 1,050 ng/dL) are achieved. The daily testosterone dose may be increased from 60 mg to 90 mg (three pump or three twist actuations) or from 90 mg to 120 mg (four pump or four twist actuations).

*Striant*

The recommended dose for Striant is the application of one buccal system (30 mg) to the gum region twice daily (60 mg/day); morning and evening (about 12 hours apart).<sup>6</sup>

## Availability

### *Androderm*

Androderm is available as a transdermal patch that delivers 2 mg/day or 4 mg/day of testosterone.<sup>1</sup> Androderm 2 mg/day is available in a carton containing 60 patches, Adroderm 4 mg/day is available in a carton containing 30 patches. Patches must be stored inside the provided pouch.

### *AndroGel (generic)*

AndroGel is available as a 1% and 1.62% gel.<sup>3,4</sup> AndroGel 1% is supplied in unit-dose aluminum foil packets in cartons of 30. Each packet of 2.5 g or 5 g gel contains 25 mg or 50 mg testosterone (25 mg/2.5 g and 50 mg/5 g), respectively. The generic AndroGel 1% gel is also available as a metered-dose pump. Each pump actuation delivers 12.5 mg of testosterone /1.25 g of gel. AndroGel 1.62% is supplied in non-aerosol, metered-dose pumps that deliver 20.25 mg of testosterone/complete pump actuation. Each 88 g metered-dose pump is capable of dispensing 75 g of gel or 60-metered pump actuations; each pump actuation dispenses 1.25 g of gel. AndroGel 1.62% is also supplied in unit-dose aluminum foil packets in cartons of 30. Each packet of 1.25 g or 2.5 g gel contains 20.25 mg or 40.5 mg testosterone (20.25 mg/1.25 g or 40.5 mg/20.25 g), respectively.

### *Fortesta (generic)*

Fortesta is available as a gel supplied in a 60 g canister with a metered dose pump that delivers 10 mg of testosterone per complete pump actuation.<sup>7</sup> The metered dose pump is capable of dispensing 120 metered pump actuations. One pump actuation dispenses 0.5 g of gel.

### *Testim (generic)*

Testim is available as a gel in a unit-dose tube in cartons of 30 tubes.<sup>2</sup> Each tube contains 50 mg of testosterone in 5 g of gel.<sup>2</sup>

### *Vogelxo (generic)*

Vogelxo is a gel supplied in unit-dose tubes or unit-dose packets each in cartons of 30.<sup>8</sup> Each tube or packet contains 50 mg testosterone/5 g of gel. Vogelxo is also supplied in a metered-dose pump that delivers 12.5 mg of testosterone/complete pump actuation. Each 88 g metered-dose pump is capable of dispensing 75 g of gel or 60-metered pump actuations. Each pump actuation delivers 12.5 mg of testosterone in 1.25 g of gel (four actuations = 50 mg testosterone). The metered-dose pump is supplied in cartons of two.

**Table 3. Vogelxo (generic) Availability.<sup>8</sup>**

Strength	Package Size
50 mg testosterone	30 tubes (5 g gel/tube)
50 mg testosterone	1 tube (5 g gel/tube)
50 mg testosterone	30 packets (5 g gel/packet)
50 mg testosterone	1 packet (5 g gel/packet)
12.5 mg of testosterone per pump actuation	2 x 75 g pumps (each pump dispenses 60 metered 1.25 g of gel)

### *Natesto*

Natesto is a nasal gel available as a metered dose pump containing 11 grams of gel dispenses as 60 metered pump actuations.<sup>9</sup> One pump actuation delivers 5.5 mg of testosterone in 0.122 g of gel (one bottle contains 10 doses of 33 mg testosterone/day).

*Testosterone 2% solution (Axiron, generic only)*

Testosterone 2% solution (Axiron, generic only) is available as a topical solution that delivers 30 mg of testosterone in 1.5 mL of solution (one pump or twist actuation).<sup>6</sup> The topical solution is available as a metered-dose pump containing 110 mL of solution and is capable of dispensing 90 mL of solution in 60 metered pump or twist actuations.

*Striant*

Striant is available as a mucoadhesive buccal system that delivers 30 mg of testosterone per system.<sup>5</sup> Striant is supplied in a package of 6 blister packs, containing 10 buccal systems per blister pack.

**POLICY STATEMENT**

This Drug Quantity Management program has been developed to prevent stockpiling, misuse and/or overuse use of the topical testosterone products. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration, unless otherwise noted below.

**Automation:** None.

**Drug Quantity Limits**

Product	Strength and Form	Maximum Quantity per Rx
Androderm <sup>®</sup> (testosterone transdermal system)	2 mg/day patch (box of 60 patches) 4 mg/day patch (box of 30 patches)	30 patches
AndroGel <sup>®</sup> 1% (testosterone 1% gel, generic only for pump)	2.5 g gel packet (25 mg testosterone)	30 packets
	5 g gel packet (50 mg testosterone)	60 packets
	Gel pump (60-metered pump actuations/75 g) [12.5 mg testosterone/1.25 g gel]	300 g
AndroGel <sup>®</sup> 1.62% (testosterone 1.62% gel, generic)	1.25 g gel packet (20.25 mg testosterone)	30 packets
	2.5 g gel packet (40.5 mg testosterone)	60 packets
	Gel pump (60-meterd pump actuations/75 g) [20.25 mg testosterone/pump actuation]	150 g
Fortesta <sup>™</sup> (testosterone 2% gel, generic)	120 metered pump actuations/60 g [10 mg testosterone/pump actuation]	120 g
Testim <sup>®</sup> (testosterone 1% gel, generic)	50 mg testosterone/5 g gel tube	60 tubes
Vogelxo <sup>™</sup> (testosterone 1% gel, generic)	50 mg testosterone/5 g gel tube	60 tubes
	50 mg testosterone/5 g gel packet	60 packets
	Gel pump (60-metered pump actuations/75 g) [12.5 mg testosterone/1.25 g gel pump actuation]	300 g
Natesto <sup>™</sup> (testosterone nasal gel)	Metered dose pump (60-metered pump actuations/pump) [5.5 mg testosterone/1.22 g gel pump actuation]	3 metered dose pump bottles (21.96 g [7.32 g/bottle x 3 bottles])
Testosterone 2% solution (Axiron, generic only)	Metered dose pump (one bottle = 90 mL solution or 60 metered pumps or twist actuations) [30 mg testosterone/1.5 mL solution]	180 mL

**Drug Quantity Limits (continued)**

Product	Strength and Form	Maximum Quantity per Rx
Striant™ (testosterone buccal system, mucoadhesive) [obsolete]	30 mg buccal system	60 buccal systems

\*This allows for a sufficient quantity for each of the products for a 30 day supply at maximum recommended doses. For coverage of additional quantities of AndroGel, Fortesta and Androderm (e.g., for dose titration, Female-to-Male gender reassignment), a coverage review is required.

**CRITERIA**

Androderm 2 mg/day transdermal patch

No overrides recommended.

Androderm 4 mg/day transdermal patch

1. If the request is for Gender-Dysphoric/Gender-Incongruent Persons/Female-to-Male (FTM) Gender Reassignment, approve 60 patches per dispensing.

AndroGel 1%, 2.5 g gel packet (generic)

1. If the dose is being titrated, approve a one-time override for the requested quantity, not to exceed 90 packets.

Note: If the dose is being titrated to > 75 mg/day, the patient should use the 5 g gel packets.

2. If the maintenance dose is 75 mg/day, approve 90 packets per dispensing.

Note: If the maintenance dose is > 75 mg/day, the patient should use the 5 g gel packets.

AndroGel 1%, 5 g gel packet (generic)

No overrides recommended.

Testosterone gel 1% gel pump (AndroGel, generic only)

No overrides recommended.

AndroGel 1.62%, 1.25 g packet (generic)

1. If the dose is being titrated, approve a one-time override for the requested quantity, not to exceed 90 packets.

Note: If the dose is being titrated to > 60.75 mg/day, the patient should use the 2.5 g gel packets.

2. If the maintenance dose is 60.75 mg/day, approve 90 packets per dispensing.

Note: If the maintenance dose is > 60.75 mg/day, the patient should use the 2.5 g gel packets.

AndroGel 1.62%, 2.5 g gel packets (generic)

No overrides recommended.

AndroGel 1.62%, gel pump (generic)

1. If the request is for Gender-Dysphoric/Gender-Incongruent Persons/Female-to-Male (FTM) Gender Reassignment, approve 225 g per dispensing.

Fortesta 2%, gel pump (generic)

1. If the request is for Gender-Dysphoric/Gender-Incongruent Persons/Female-to-Male (FTM) Gender Reassignment, approve 180 g per dispensing.

Testim 1% gel, 5 g tube (generic)

No overrides recommended.

Vogelxo 1% gel, 5 g tube, 5 g packet, and gel pump (generic)

No overrides recommended.

Natesto nasal gel pump

No overrides recommended.

Testosterone 2% topical solution metered-dose pump (Axiron, generic only)

No overrides recommended.

Striant mucoadhesive buccal system

No overrides recommended.

## REFERENCES

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