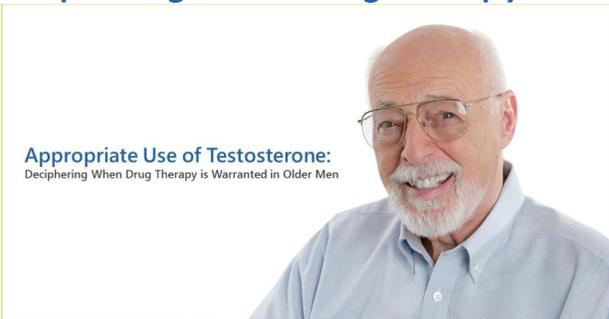




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## Appropriate Use of Testosterone: Deciphering When Drug Therapy is Warranted in Older Men

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This activity will discuss when testosterone replacement therapy is clinically indicated as well as how help personalize therapy based on a variety of formulations. Side effects and monitoring will also be discussed to equip healthcare practitioners with the tools necessary to improve patient care for patients considering or receiving testosterone replacement therapy.

### Learning Objectives

#### Pharmacist

- 1 Determine when testosterone therapy is deemed appropriate vs inappropriate
- 2 Describe the advantages and limitations associated with various testosterone formulations
- 3 Identify monitoring parameters and potential side effects associated with testosterone replacement therapy

#### Pharmacy Technician

- 1 Recognize when testosterone therapy is deemed appropriate vs inappropriate
- 2 Describe the advantages and limitations associated with various testosterone formulations
- 3 Recognize when to alert the pharmacist regarding patient complaints of side effects potentially associated with testosterone replacement therapy

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## Introduction

As men age, the amount of testosterone naturally produced by the body declines which can lead to a presentation of signs and symptoms including decline in sexual function, limitations in mobility, and a decrease in energy. Past trials have yielded inconsistent results regarding the benefit associated with testosterone use in the clinically symptomatic older male population, but recently published trials have shed some light on safety and efficacy of testosterone replacement therapy. As healthcare practitioners, it is important to be able to determine when testosterone supplementation is deemed clinically appropriate, know how to counsel patients on a variety of testosterone formulations, and know what and when to monitor and look for when patients begin or continue therapy considering a rapid increase in prescriptions for testosterone products has taken place in part due to the marketing of various formulations.<sup>1</sup>

Goals of testosterone replacement therapy include improvement of sexual function, maintenance of secondary sex characteristics, improvement of bone mineral density, and to achieve a better sense of overall well-being. Data from older studies revealed an increase in muscle mass and a decrease in fat related to exogenous testosterone replacement therapy but did not find a correlation to an increase in energy, sexual function, or physical performance.<sup>2</sup> Male hypogonadism has been the main indication for testosterone use for years, but contrary to earlier research, studies are now being published regarding the potential benefits for cosmetic purposes such as sexual function, physical appearance and performance, and vitality. Current FDA approved indications for testosterone replacement therapy in older men include primary hypogonadism and hypogonadotropic hypogonadism.<sup>1</sup> There are three major physiological mechanisms by which testosterone levels can be lower than normal. Primary hypogonadism occurs when testosterone levels are low due to hypothalamic-pituitary-testicular axis abnormalities at the level of the testicles which results in elevated LH and FSH and low testosterone levels. Hypogonadotropic hypogonadism, or secondary hypogonadism, is associated with abnormalities of the hypothalamic-pituitary-testicular axis at the level of the pituitary gland or hypothalamus which results in normal LH levels but a low serum testosterone. Hypogonadotropic hypogonadism leads to a low level in testosterone due to gonadal failure caused by abnormal pituitary gonadotropin levels.<sup>3</sup> In this case, gonadal failure develops as a result of the pituitary failing to secrete gonadotropin or as a result of insufficient hypothalamic secretion of gonadotropin releasing hormone. Causes include harm to the hypothalamus or pituitary gland by tumor, radiation, or surgery, iron overload, chronic glucocorticoid or opioid use, among others.<sup>4</sup>

Fatigue, severe depression, difficulty concentrating, sexual dysfunction, and loss of strength and muscle mass are all signs and symptoms of androgen deficiency. Diagnosis is made based on signs and symptoms, serum testosterone level, and sex hormone-binding globulin. Serum testosterone is considered low when levels are below 300 ng/dL.<sup>2</sup> If levels are below 300 ng/dL but the patient is not experiencing clinical signs and symptoms, it is not deemed necessary to treat the number since a diagnosis is made based on serum

testosterone level and signs and symptoms associated with androgen deficiency. In addition to checking serum testosterone levels, adverse reactions related to product-specific agents should be monitored.

Therapy is deemed appropriate in men who are 65 years old or older with signs and symptoms associated with androgen deficiency, a testosterone level below 275 ng/dL, and no contraindications to therapy such as a history of prostate cancer or occurrence of a cardiovascular event within the past three months.<sup>1,5</sup> Choice of product or formulation is dependent upon patient-specific characteristics, preferred or appropriate route of administration, and monitoring parameters.

### **Patient Population Treatment Precautions**

Testosterone replacement therapy should be avoided in patients with any history of prostate or breast cancer due to potential for exacerbating symptoms, cancer growth, or recurrence. Although breast cancer is less common in men than women, 1/1000 men experience a battle with breast cancer.<sup>6</sup> Treatment should also be avoided in patients with a prostate nodule, lower urinary tract symptoms, prostate specific antigen (PSA) greater than 4 ng/dL, and PSA greater than 3 ng/dL with increased risk of developing prostate cancer. Populations at increased risk include African Americans or patients with first-degree relatives with prostate cancer. Precaution is taken in this patient population to avoid prostate growth, risk of prostate cancer, and to prevent lower urinary tract symptoms such as incomplete urination. It is recommended to avoid testosterone therapy if patients have a baseline hematocrit greater than 50 percent because of potential increased risk of cardiovascular events already placed on this population. By supplementing this patient population with exogenous testosterone, red blood cell mass may increase as well as multiply leading to an increase in blood viscosity. This decreases cerebral perfusion therefore leading to potential for thrombosis and stroke.<sup>2,5</sup>

### **Comorbid Conditions Associated with Low Testosterone**

Patients with type II diabetes are twice as likely to develop low serum testosterone. Inverse relationships have been found between BMI and testosterone, waist-to-hip ratio and testosterone, and sex-hormone binding globulin and testosterone.<sup>7</sup> This is an opportunity that few pharmacists acknowledge and one where many can make a difference. Counseling obese and diabetic patients on exercise and weight loss may be helpful in making strides toward increasing serum testosterone through nonpharmacologic methods. Not only would eating healthier and increasing exercise be beneficial in regards to the management of their disease states, but these lifestyle modifications would also help to naturally increase endogenous testosterone levels. A thorough drug regimen review should take place prior to beginning exogenous testosterone therapy to account for any medications that may cause a low testosterone level or symptoms associated. Two classes of

medications that are frequent culprits are opioids and glucocorticoids. In a normal feedback loop, low testosterone would send a signal to the hypothalamus to release gonadotropin releasing hormone. This would then send a signal to the anterior pituitary to secrete LH and FSH which would then send signals to the testes to produce and release testosterone into the blood.<sup>8</sup> Opioids suppress the hypothalamic-pituitary-gonadal axis which can cause symptoms of androgen deficiency, particularly methadone because of its long duration of action. A longer duration of action means longer suppression.<sup>2</sup> Glucocorticoids may also cause testosterone levels to drop below the lower limit of normal due to suppression of the hypothalamic-pituitary-testicular axis at the level of the pituitary gland and possibly preventing the hypothalamus from releasing gonadotropin releasing hormone.<sup>9</sup> It is recommended to offer testosterone replacement therapy to men receiving high doses of glucocorticoids who already have low levels of serum testosterone to maintain lean body mass and bone mineral density.<sup>2</sup>

One-fifth to one-quarter of men with HIV have low testosterone. Low testosterone in this population is associated with disease progression and decline in overall health. It is recommended to offer short-term testosterone replacement therapy for three to six months to patients with weight loss associated with HIV and low levels of testosterone with a goal of maintaining a healthy weight, lean body mass, and strength.<sup>2</sup>

While many older patients are not concerned with fertility, it is still important to consider the effects for those who are concerned. Low testosterone can lead to infertility; however, treating patients experiencing low testosterone and infertility with exogenous testosterone can lead to worsening symptoms over time. Short-term therapy may alleviate some of the symptoms, but long-term therapy may cause the body to stop producing any amount of endogenous testosterone due to shutting off the feedback loop. As testosterone levels appear to remain within range due to exogenous testosterone administration, the hypothalamus stops releasing gonadotropin releasing hormone; therefore, the testes stop sending feedback signals leading to reduction in endogenous testosterone production.<sup>2</sup>

## **FDA Approved Formulations**

Over a matter of four years, the money spent on testosterone replacement therapy doubled and is expected to continue growing.<sup>10</sup> With so much direct-to-consumer advertising, patients are becoming more aware of the products that are available which contributes to the increased growth of testosterone replacement therapy. This also presents pharmacists with new opportunities to help optimize and individualize therapy. A variety of testosterone formulations have made their way to the market which helps to individualize therapy based on patient-specific needs and attributes. While some forms of drug delivery offer ease of use with topical application or self-administration with oral preparations, several factors must be considered to prevent harm from being done to the patient.

## Oral Preparations

US approved oral testosterone preparations include fluoxymesterone (Androxy), and methyltestosterone (Android, Methitest, and Testred). Testosterone formulated into an oral medication certainly offers some advantages such as autonomous self-administration, the ability to immediately discontinue the medication and its effects within a few hours, and flexibility with dosing. Disadvantages of this route of administration include variable pharmacokinetic properties and response between patients. Patients must also remember to take the medication daily. This preparation is not recommended for use and will not be appropriate for the vast majority of patients due to potential for hepatotoxicity. The risk of hepatotoxicity is greatly increased with the oral route versus the other routes due to being a substrate of liver enzymes unlike any of the other formulations.<sup>2,11</sup>

## Parenteral Preparations

Parenteral preparations include testosterone cypionate (Depo-Testosterone), testosterone enanthate (Delatestryl), and testosterone undecanoate (Aveed – US only). Advantages of testosterone cypionate and testosterone enanthate include infrequent administration, typically every one to two weeks, due to the long-acting formulation, low cost, and ability to initiate and maintain normal levels in hypogonadal men. Disadvantages include more dynamic changes in testosterone levels when compared to agents applied or taken daily. This may cause more pronounced symptoms due to administration of a large amount of drug at once. Effects of therapy with this formulation wane after two or three weeks. It is recommended to administer 75-100 mg weekly or 150-200 mg every other week to maintain consistent levels.<sup>2,12</sup>

Advantages to testosterone undecanoate include injections administered even less frequently than testosterone cypionate and testosterone enanthate, less fluctuation in testosterone level due to its ultra-long-acting formulation, and no adjustments in dose due to such slow release. While testosterone undecanoate offers convenience with maintenance administration occurring every 10 weeks, there are disadvantages and considerations to be mindful of including the large volume of drug injected intramuscularly, the cost toxicity associated leading to inability of some patients to afford the product, and the possibility of anaphylaxis and pulmonary microembolism. This form of the long-acting parenteral testosterone products comes with a REMS program due to the potential for anaphylaxis and serious pulmonary oil microembolism. This means that prescribers must be certified and qualified to administer this specific testosterone product, and patients must remain under observation for a half hour after the medication has been administered.<sup>1,13</sup>

## Transdermal Patch

Androderm is a transdermal formulation that allows patients to apply one testosterone containing patch every 24 hours. The patch must be removed and replaced with a new patch each evening. Sites of application include a hairless area located on the back, thighs, abdomen, or upper arms, and as with all topical forms of testosterone should NEVER be applied to the genital area. It is not recommended to apply to a bony area or to an area of the body that is subject to prolonged periods of pressure such as when sitting or sleeping due to poor blood flow. The patch should not be applied to an area of skin that is irritated, broken, or oily due to potential for excess drug delivery, aggravating the skin, or trouble keeping the product in contact with the skin. Sites of application should be rotated daily, not using the same site for a period of 7 days or more. An often missed counseling point is that patients should not expose the newly applied patch to water for at least three hours after application. This formulation is advantageous because of its convenience, ease of use, and ability to mimic the body's diurnal testosterone pattern. On the contrary, discontinuation may occur due to more than one-third of patients experiencing skin reactions associated with the patch. If the patient experiences skin reactions, over-the-counter low potency steroid cream should help soothe the inflammation and irritation associated. The other disadvantage of this formulation is a higher cost associated than with the intramuscular products.<sup>14</sup>

## Gels and Transdermal Solution

AndroGel 1%, AndroGel 1.62% (US only), Fortesta 2% (US only), and Testim 1% are topical gel testosterone products that are application friendly but caution must be used to prevent transfer from patient to other subjects such as cohabitants, children, and pets. These gels cause skin reactions and irritation to a lesser degree compared to patches, and with slow, constant exposure to testosterone, these products are formulated to provide the body with more consistent levels and less fluctuation in testosterone levels. These products are not to be applied to the genital area. Patients should be instructed to apply the gel or solution each morning to the upper arms or shoulders. It is recommended to apply Fortesta 2% to the thighs rather than upper arms or shoulders, and AndroGel 1% may also be applied to the abdomen.<sup>2,14</sup>

Axiron 2% is a topical solution that is applied to the underarms each morning. It is recommended to apply deodorant prior to use of Axiron 2%. This medication offers the same advantages and disadvantages as the other transdermal gels.<sup>2,14</sup>

## Pellet

Testopel is testosterone in the form of pellets which are placed subcutaneously every three to six months by a physician. The pellets are implanted into the thigh, buttocks,

or lower abdomen using a local anesthetic. This dosage form is advantageous due to the convenience offered by its long-acting properties and infrequency of dosing. However, the pellets are each 75 mg which does not lend much flexibility with dosing adjustments. Prior to initiating therapy with Testopel, patients can achieve a therapeutic dose of testosterone with an intramuscular formulation and use that dose when converting to the pellets.<sup>1</sup> After insertion of the pellets, patients may ice the site of implantation for 20 to 30 minutes every hour as needed for discomfort, pain, or swelling.<sup>15</sup> Cost is an important consideration as well as commitment of follow-up appointments.

## **Buccal**

Striant is a buccal formulation of testosterone and is approved for use in the United States only. This product is formulated to be slowly absorbed by applying one tablet to the gums above one of the front incisor teeth where it will take the shape of the gum area and stay in place. Directions for use are to use one tablet every 12 hours. Buccal tablets should not be chewed or swallowed. The buccal system is not designed to dissolve entirely, so the old tablet must be removed prior to placement of a new tablet. This dosage form is not impacted by eating or chewing gum, and is not affected by drinking though the tablet should be removed prior to morning and evening oral care.<sup>14</sup>

## **Nasal Gel**

Natesto is a metered dose formulation of testosterone that is used three times daily. By placing the gel in an area that is less exposed, there is minimal risk of transfer to others. Prior to administering therapy, patients should blow their nose. The pump should be primed by inverting the device and pressing the pump down ten times. One actuation should be administered into each nostril. Afterward, it is recommended to gently massage the nostrils slightly below the bridge of the nose, and patients should be instructed to abstain from sniffing or blowing nose for an hour. If any product comes in contact with the hands, washing with warm water and soap should immediately take place. While this product may be appropriate for many patients, cost and frequency of administration must be considered prior to therapy initiation with this product.<sup>14</sup>

## **Side Effects and Monitoring**

With a wide realm of testosterone replacement therapies, each dosage form comes with specific side effects in addition to the class-wide monitoring parameters. Some possible class-wide adverse events associated with testosterone include an increase in PSA, prostatitis, redness and itching at the site of topical application, arthralgia, skin oiliness and acne, and a bump in hematocrit.<sup>2</sup>

Monitoring testosterone levels and other dynamic parameters during treatment is necessary to ensure goal levels are reached and maintained with minimal side effects. During treatment, lipid panels, liver function tests, and hemoglobin and hematocrit should be measured at three to six months after therapy initiation and then annually. If hematocrit rises above 54 percent, therapy must be discontinued due to risk of thrombosis and stroke. Glucose readings in diabetic patients need to be monitored since insulin sensitivity and levels of testosterone show a positive correlation. If a patient is more sensitive to exogenous or endogenous insulin, it is likely that their testosterone level may be more elevated than a patient who is less sensitive to insulin, or vice versa. The correlation between insulin sensitivity and serum testosterone is not entirely understood, and additional studies would need to be performed to determine which is the cause and which is the effect. Any patient taking exogenous testosterone must be monitored for cardiovascular events, such as stroke and myocardial infarction, throughout and after discontinuation of therapy. Bone mineral density should be checked in men with low testosterone and osteoporosis one to two years after therapy initiation, though these products have not shown to increase risk of fractures. An increase in PSA is an indicator that the prostate is growing. For patients older than 40 who had a baseline PSA greater than 0.6 ng/mL, PSA should be drawn and a prostate exam should take place three to six months after starting therapy and then according to The Endocrine Society's Clinical Guidelines.<sup>2</sup> In addition to specific monitoring parameters, healthcare practitioners should look for signs of testosterone dependence such as attempting to refill prescriptions early on multiple occasions or patients obtaining testosterone prescriptions from multiple prescribers.

### **Oral Preparations Monitoring/Side Effects**

Oral preparations of testosterone come with adverse effects related to the organs involved in metabolism. They can cause adverse changes in lipids and damage to the liver which is why these products are not recommended in the US. By taking oral testosterone, patients are at higher risk for hepatotoxicity with effects including cholestasis, transaminases abnormally high, cysts within the liver, and hepatocellular carcinoma. It is recommended to obtain a testosterone level five hours after administration and prior to taking the next dose.<sup>2,11</sup> Oral testosterone is not first choice for older males experiencing hypogonadism, but it may be used in women experiencing poor sexual function, in women to help prevent osteoporosis, and to help treat psychological symptoms in women such as depression.<sup>16</sup>

### **Parenteral Preparations Monitoring/Side Effects**

As with any injectable medication, testosterone cypionate, testosterone enanthate, and testosterone undecanoate IM may cause symptoms associated with pain at the injection site such as redness or itching. Other side effects to monitor for when taking these medications include an increase in red blood cell mass and hematocrit, and a rare cough

after medication injection. Testosterone should not be given if a baseline hematocrit is greater than 50 percent due to risk of cardiovascular related adverse events. Levels for patients using testosterone cypionate or testosterone enanthate should be drawn mid-way between injections.<sup>2,11,17</sup>

While testosterone undecanoate offers convenience because of infrequent administration associated with this product, there is potential for anaphylactic reaction and pulmonary oil microembolism which could lead to death. For patients using testosterone undecanoate, levels should be checked three months after therapy initiation, five weeks after administration of the third dose, and then annually with each physician visit.<sup>2</sup> It is important to educate patients on the side effects to inform them of the potential risks and to consider the patient's commitment to follow-up monitoring prior to initiating therapy.

### **Transdermal Patch Monitoring/Side Effects**

As a transdermal patch, Androderm offers ease of use and user friendly administration. Directions for use are to remove the old patch after 24 hours and replace with a new patch each evening. The downfall to using patches is the potential for skin reactions which may lead to discontinuation, typically occur in about one-third of patients. Upon removal of a patch, if mild skin irritation is present, patients may use OTC hydrocortisone cream 1%. It is not advised to use topical steroid ointments due to their oily properties and difficulty with patch application when the next dose is due. Serum testosterone levels should be measured three to twelve hours after applying the patch at a follow-up appointment three months after therapy initiation, and then annually.<sup>14,17</sup>

### **Transdermal Gels and Solutions Monitoring/Side Effects**

While topical gels and solutions do not cause as much skin irritation as patches, the concern of product transfer arises. Administration is convenient; however, it is easy to spread the product to others, especially cohabitants, children, and pets. Two of the most strategic ways to combat medication transfer are by washing hands after topical application and to cover the site of application with clothing as soon as the gel or solution has dried. According to the Endocrine Society's Clinical Guidelines, testosterone levels should be monitored after at least one week of use, and doses should be adjusted to reach a serum testosterone in the mid-normal range.<sup>2</sup>

Each product has specific monitoring parameters:

AndroGel 1%: about 14 days after initiation or dose adjustments<sup>14</sup>

AndroGel 1.62%: 14-28 days after initiation or dose adjustments<sup>14</sup>

Fortesta: measure levels two hours after applying and 14-35 days after initiation or adjustments<sup>14</sup>

Testim: measure morning levels after 14 days of therapy or after dose adjustment<sup>14</sup>

Axiron: two to eight hours after applying and 14 days after therapy initiation or dose adjustments<sup>14</sup>

### **Pellet Monitoring/Side Effects**

Testopel is convenient for patients because it requires infrequent administration; however, some disadvantages to this formulation include inability to self-administer, pain, redness, and inflammation at the site of implantation, possibility of pellet extrusion, fibrosis, and infection<sup>11</sup>. Serum testosterone levels should be monitored after each dosing interval<sup>17</sup>. Commitment to follow-up monitoring should be assessed prior to therapy initiation.

### **Buccal Monitoring/Side Effects**

Striant comes in 30 mg buccal tablets which take the shape of the patient's gums upon application and remains in place for 12 hours until change is warranted. While this product allows testosterone levels to remain fairly constant without great fluctuation, it can cause irritation in the mouth and on the gums, and some patients experience changes in taste. It is recommended to examine the areas of the gums where the tablets are applied and to monitor morning testosterone levels four to 12 weeks after the start of therapy. Treatment should be discontinued if levels are repeatedly outside of normal limits (300-1,050 ng/dL).<sup>14</sup>

### **Nasal Monitoring/Side Effects**

Natesto is an intranasal formulation of testosterone that requires one actuation in each nostril three times a day, usually separated by six to eight hours. Alternative therapy should be considered in patients who have allergies or nasal and sinus pathology due to potential for exacerbation of symptoms.<sup>11</sup> Possible side effects include sinusitis and rhinorrhea, discomfort or scabbing along the nasal pathway, and nasopharyngitis. After patients have been on therapy for one month, serum testosterone levels should be checked periodically. If levels are greater than 1,050 ng/dL on multiple accounts, therapy should be discontinued. If testosterone levels are consistently <300 ng/dL, alternative therapies should be explored.<sup>14</sup>

### **Conclusion**

Exogenous testosterone offers benefit to symptomatic older men with sexual dysfunction, decreased vitality, and a decline in physical function according to recently

published evidence,<sup>1</sup> but therapy should be avoided in patients with cardiovascular risk factors,<sup>5</sup> elevated prostate specific antigen, or hematocrit greater than 50 percent<sup>1</sup>. Though testosterone replacement therapy is only FDA approved for primary hypogonadism and hypogonadotropic hypogonadism,<sup>2</sup> studies have illustrated statistically significant improvements in sexual dysfunction ( $p < 0.001$ ), physical function ( $p = 0.003$ ), and vitality ( $p = 0.006$ ).<sup>1</sup> Target testosterone levels are 275-300 ng/dL or greater,<sup>1,2</sup> and if levels consistently remain low, a change in therapy should be considered.<sup>14</sup> With an increase in prescribing, it is crucial to be able to appropriately recommend a product formulation to a physician based on patient-specific characteristics, and be able to counsel patients on side effects, monitoring, and route of administration. Monitoring of testosterone levels, for adverse events, and for appropriateness of therapy is crucial prior to and during treatment. In conclusion, testosterone replacement therapy should not be administered simply because of age or solely based on a low level, but therapy should be individualized based on consideration of serum testosterone level, signs and symptoms of androgen deficiency, and patient-specific disease states.

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### **Appropriate Use of Testosterone: Deciphering When Drug Therapy is Warranted in Older Men • April 2019 • Volume 41, #4**

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CPE Monitor ePID \_\_\_\_\_

BIRTHDATE (MM/DD) \_\_\_\_\_

IF LICENSED IN FLORIDA, FL LICENSE # \_\_\_\_\_

EMAIL ADDRESS \_\_\_\_\_

**LESSON EVALUATION**

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1a. **PHARMACISTS ONLY:** Does this lesson meet the learning objectives? (Circle choice).

- Determine when testosterone therapy is deemed appropriate vs inappropriate YES NO
- Describe the advantages and limitations associated with various testosterone formulations YES NO
- Identify monitoring parameters and potential side effects associated with testosterone replacement therapy YES NO

1b. **TECHNICIANS ONLY:** Does this lesson meet the learning objectives? (Circle choice).

- Recognize when testosterone therapy is deemed appropriate vs inappropriate YES NO
- Describe the advantages and limitations associated with various testosterone formulations YES NO
- Recognize when to alert the pharmacist regarding patient complaints of side effects potentially associated with testosterone replacement therapy YES NO

2. Was the program independent & non-commercial? YES NO

3. Relevance of topic

	Low Relevance					Very Relevant	
	1	2	3	4	5	6	7

4. What did you like **MOST** about this lesson? \_\_\_\_\_

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5. What did you like **LEAST** about this lesson? \_\_\_\_\_

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6. How would you improve this lesson? \_\_\_\_\_

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**PLEASE MARK THE CORRECT ANSWER(S)**

- 1. Which product should be avoided in a patient with eczema?**
  - a. Striant
  - b. Androderm
  - c. Depo-Testosterone
  - d. Natesto
- 2. When should serum testosterone levels be drawn for a patient receiving testosterone cypionate every two weeks?**
  - a. One week after injection
  - b. Five weeks after the third injection
  - c. Five hours after administration
  - d. Immediately prior to the next dose
- 3. In which patient population is therapy deemed inappropriate?**
  - a. Baseline hematocrit of 45%
  - b. Weight loss associated with HIV
  - c. Baseline PSA greater than 4 ng/mL
  - d. Patient being treated for obstructive sleep apnea
- 4. What is an appropriate goal level for serum testosterone?**
  - a. 4 ng/mL
  - b. 100 ng/dL
  - c. 250 ng/dL
  - d. 350 ng/dL
- 5. Which therapy would be least appropriate for a patient with a busy lifestyle who may forget medication administration easily?**
  - a. a. Natesto

- b. b. Delatestryl
  - c. c. Androderm
  - d. d. Methitest
6. All the following are potential side effects of exogenous testosterone replacement therapy EXCEPT:
- a. Acne
  - b. Infertility
  - c. Potential for stroke or thrombosis
  - d. Increased risk for bone fractures
7. Which product has a REMS program regarding anaphylaxis and potential for serious pulmonary oil microembolism associated with it?
- a. Aved
  - b. Depo-Testosterone
  - c. Delatestryl
  - d. Methitest
8. While skin irritation is a potential side effect of Androderm, which of the following is recommended to combat mild topical irritation?
- a. Benadryl
  - b. Cold compress
  - c. Hydrocortisone 1% cream
  - d. Triamcinolone 0.1% ointment
9. What would be an appropriate dose of testosterone cypionate?
- a. 100 mg every other week
  - b. 150 mg weekly
  - c. 200 mg weekly
  - d. 150 mg every other week
10. Where is an appropriate site of application for Axiron 2%?
- a. the abdomen
  - b. the genitals
  - c. under the arms
  - d. the thighs