PRODUCT MONOGRAPH

Testosterone USP

Transdermal Delivery System, 12.2 mg and 24.3 mg

Androgens

Allergan Inc.
85 Enterprise Blvd. Suite 500
Markham, Ontario
L6G 0B5
www.allergan.ca

Date of Preparation:
February 28, 2018

Submission Control No: 213105

Table of Contents

ANDRODERM®

Testosterone

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Transdermal	Patches 12.2 mg and 24.3 mg	Alcohol, purified water, glycerin, glycerol monooleate, methyl laurate, carbomer, and sodium hydroxide. *For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

Androderm is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone (hypogonadism).

Androderm should not be used to treat non-specific symptoms suggestive of hypogonadism if testosterone deficiency has not been demonstrated and if other etiologies responsible for the symptoms have not been excluded. Testosterone deficiency should be clearly demonstrated by clinical features and confirmed by two separate biochemical assays (morning testosterone) before initiating therapy with any testosterone replacement, including Androderm treatment.

Geriatrics (>65 years of age):
There are limited controlled clinical study data supporting the use of Androderm in the geriatric population (see WARNINGS AND PRECAUTIONS and CLINICAL TRIALS).

Paediatrics (<18 years of age):
Androderm is not indicated for use in children < 18 years of age since safety and efficacy have not been established in this patient population (see WARNINGS AND PRECAUTIONS – Special Populations).

CONTRAINDICATIONS

- Androderm is not indicated for use in women.

- Pregnant and nursing women should avoid skin contact with Androderm application sites on men. Testosterone may cause fetal harm. Testosterone exposure during pregnancy has been reported to be associated with fetal abnormalities (see WARNINGS AND PRECAUTIONS – Special Populations). In the event that unwashed or unclothed skin to which Androderm® has been applied or clothing exposed to Androderm comes in direct contact with the skin of a pregnant or nursing woman, the general area of contact on the woman should be immediately washed with soap and water.

- Androgens are contraindicated in men with known or suspected carcinoma of the prostate or breast.

- Androderm should not be used in patients with known hypersensitivity to any of its ingredients, including testosterone USP that is chemically synthesized from soy. Androderm should be used with caution by men with a previous history of photosensitivity or hypersensitivity to topically applied medications and by those individuals who have been sun burnt in the proposed area of application within three weeks prior to the initiation of therapy. For a complete listing, see Dosage Forms, Composition and Packaging section of the Product Monograph.

WARNINGS AND PRECAUTIONS

General

There is very limited data from clinical trials with Androderm in the geriatric male (>65 years of age) to support the efficacy and safety of prolonged use. Impacts to prostate and cardiovascular event rates and patient important outcomes are unknown[8].

Androderm should not be used to attempt to improve body composition, bone and muscle mass, increase lean body mass and decrease total fat mass. Efficacy and safety have not been established. Serious long term deleterious health issues may arise.

Androderm has not been shown to be safe and effective for the enhancement of athletic performance. Because of the potential risk of serious adverse health effects, this drug should not be used for such purpose.

If testosterone deficiency has not been established, testosterone replacement therapy should not be used for the treatment of sexual dysfunction.

Testosterone replacement therapy is not a treatment for male infertility.

Transfer of testosterone to another person can occur when skin-to-skin contact is made with the application site.

The following precautions are recommended to minimize potential transfer of testosterone from Androderm treated skin to another person:

- Patients should wash their hands thoroughly and immediately with soap and water after application of Androderm. Topically applied testosterone can be removed from the skin surface by thorough washing with soap and water.

- Direct skin-to-skin contact should be avoided immediately following administration of a topical testosterone product. Prior to any situation in which direct skin-to-skin contact is anticipated, patients should wash the application sites thoroughly with soap and water so as to remove drug residue.

- In the event that unwashed or unclothed skin to which Androderm has been applied does come in direct contact with the skin of another person, the general area of contact on the other person should be washed thoroughly with soap and water as soon as possible.

Skin burns have been reported at the patch site in patients wearing an aluminised transdermal system during a magnetic resonance image scan (MRI). Because Androderm contains aluminium it is recommended to remove the system before undergoing an MRI.

Special Populations

Pregnant Women and Nursing Women:
Pregnant and nursing women should avoid skin contact with Androderm application sites on men. Testosterone may cause fetal harm. Testosterone exposure during pregnancy has been reported to be associated with fetal abnormalities. In the event that unwashed or unclothed skin to which Androderm has been applied or clothing exposed to Androderm comes in direct contact with the skin of a pregnant or nursing woman, the general area of contact on the woman should be immediately washed with soap and water (see CONTRAINDICATIONS).

Paediatrics (<18 years of age):
Androgen therapy should be used cautiously in males with hypogonadism causing delayed puberty. Androgens can accelerate bone maturation without producing compensatory gain in linear growth. This adverse effect may result in compromised adult stature. The younger the child is the greater risk of compromising final mature height. The effect of androgens on bone maturation should be monitored closely by assessing bone age of the wrist and hand on a regular basis.

Geriatrics (> 65 years of age):
There are very limited controlled clinical study data supporting the use of testosterone in the geriatric population and virtually no controlled clinical studies on subjects 75 years and over.
Geriatric patients treated with androgens may be at an increased risk for the development of prostatic hyperplasia and prostatic carcinoma.

Geriatric patients and other patients with clinical or demographic characteristics that are

recognized to be associated with an increased risk of prostate cancer should be evaluated for the presence of prostate cancer prior to initiation of testosterone replacement therapy.

In men receiving testosterone replacement therapy, surveillance for prostate cancer should be consistent with current practices for eugonadal men.

Carcinogenesis

Prostatic:
Geriatric patients treated with androgens may be at an increased risk for the development of prostatic hyperplasia and prostatic carcinoma (see Special Populations - Geriatrics).

Breast:
Patients using long-term androgen therapy may be at an increased risk for the development of breast cancer[9].

Hepatic:
Prolonged use of high doses of orally active 17-alpha-alkyl androgens (e.g., methyltestosterone) has been associated with serious hepatic adverse effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, and jaundice). Peliosis hepatis can be a life-threatening or fatal complication. Long-term therapy with testosterone enanthate, which elevates blood levels for prolonged periods, has produced multiple hepatic adenomas.

Skeletal:
Patients with skeletal metastases are at a risk of exacerbating hypercalcemia/ hypercalciuria with concomitant androgen therapy.

Cardiovascular
Testosterone may increase blood pressure and should be used with caution in patients with hypertension.

Edema, with or without congestive heart failure, may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease. Diuretic therapy may be required, in addition to discontinuation of the drug.

Post-market studies suggest increased risk of serious cardiovascular events such as myocardial infarction and stroke associated with testosterone therapy. Before starting testosterone therapy, patients should be assessed for any cardiovascular risk factors (e.g., existing ischaemic heart disease) or prior history of cardiovascular events (e.g., myocardial infarction, stroke, or heart failure). Patients should also be closely monitored for possible serious cardiovascular events while on testosterone therapy.

Dependence/Tolerance
Androderm contains testosterone, a Schedule G controlled substance as defined by the Food and Drugs Act.

Endocrine and Metabolism
Androgens have been shown to alter glucose tolerance tests. Diabetics should be followed carefully and the insulin or oral hypoglycemic dosage adjusted accordingly (see Drug-Drug Interactions).

Hypercalciuria/hypercalcemia (caused by malignant tumours) may be exacerbated by androgen treatment. Androgens should be used with caution in cancer patients at risk of hypercalcemia (and associated hypercalciuria). Regular monitoring of serum calcium concentrations is recommended in patients at risk of hypercalciuria/ hypercalcemia.

Hypercalcemia may occur in immobilized patients. If this occurs, the drug should be discontinued.

Hematologic
Hemoglobin and hematocrit levels should be checked periodically (to detect polycythemia) in patients on long-term androgen therapy (see Monitoring and Laboratory Tests).

Alkylated derivatives of testosterone such as methandrostenolone, have been reported to decrease the anticoagulant requirement of patients receiving oral anticoagulants (e.g. warfarin). Patients receiving oral anticoagulants therapy require close monitoring, especially when androgens are started or stopped (see Drug-Drug Interactions).

Respiratory
The treatment of hypogonadal men with testosterone may potentiate sleep apnea, particularly for those with risk factors such as obesity or chronic lung diseases.

Sexual Function/Reproduction
Gynecomastia may frequently develop and occasionally persist in patients being treated for hypogonadism.

Priapism or excessive sexual stimulation may develop.

Oligospermia may occur after prolonged administration or excessive dosage.

Skin
Changes in body hair distribution, significant increase in acne, or other signs of virilization of the female partner or in any person (including children) exposed to skin-to-skin contact, should be brought to the attention of a physician.

Application site reactions associated with the use of transdermal testosterone may manifest as skin irritation (including erythema, induration or burning).

Monitoring and Laboratory Tests
The patient should be monitored (including serum testosterone levels) on a regular basis to ensure adequate response to treatment.

Currently there is no consensus about age specific testosterone levels. The normal serum testosterone level for young eugonadal men is generally accepted to be approximately 10.4-34.6 nmol/L (300-1000 ng/dL). It should be taken into account that physiological testosterone levels (mean and range) decrease with increasing age.

The following laboratory tests, performed routinely, are recommended to ensure that adverse experience possibly caused by or related to testosterone replacement therapy is detected and addressed:

- Hemoglobin and hematocrit levels should be checked periodically (to detect polycythemia);
- liver function tests; to detect hepatotoxicity associated with the use of 17-alpha-alkylated androgens;
- prostate specific antigen (PSA), Digital Rectal Examination (DRE), especially if the patient presents with progressive difficulty with urination or a change in voiding habits;
- lipid profile, total cholesterol, LDL, HDL, and triglycerides;
- Diabetics should be followed carefully and the insulin or oral hypoglycemic dosage adjusted accordingly (see Drug-Drug Interactions).

ADVERSE REACTIONS

Adverse Drug Reaction Overview

In clinical studies of 122 patients treated with Androderm®, the most common adverse events reported were skin reactions at the site of patch application. Transient mild to moderate erythema was observed at the site of application in the majority of patients at some time during treatment.

The adverse reactions reported by more than 1% of patients are listed below shown in order of decreasing frequency (Table 1).

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Table 1: Adverse reactions reported by more than 1% of patients

	Androderm® n= 122 (%)
Pruritus at Application site	39%
Burn-like blister reaction under patch	12%
Erythema at application site	8%
Vesicles at application site	6%
Prostate abnormalities	5%
Headache	5%
Allergic contact dermatitis to the patch	4%
Burning at application site	3%
Induration at application site	3%
Depression	3%
Bullae at application site	3%
Rash	2%
Gastrointestinal bleeding	2%
Pruritus	2%
Decreased libido	2%

Three types of application site reactions occurred: irritation which included mild to moderate erythema, induration or burning; allergic contact dermatitis; and burn-like blister reactions.

Chronic skin irritation caused 5% of patients to discontinue treatment.

Five patients (4%) developed allergic contact dermatitis after 3 to 8 weeks treatment that required discontinuation. These reactions were characterized by pruritus, erythema, induration and in some instances vesicles or bullae, which recurred with each patch application. Rechallenge with components of the patch showed ethanol sensitization in 4 patients. One patient's reaction was attributed to testosterone. None of these patients had adverse sequelae related to oral alcohol ingestion or to injectable testosterone use. Older patients may be more prone to develop allergic contact dermatitis.

Fifteen patients (12%) had burn-like blister reactions that involved bullae, epidermal necrosis or the development of ulcerated lesions. These reactions typically occurred once, at a single application site; 5 patients experienced a single recurrence. None withdrew from the clinical trials. These reactions occurred at a rate of approximately 1 in 6,500 patch applications (1 in

3,250 treatment days). The majority of these lesions were associated with patch application over bony prominences or on parts of the body that may have been subject to prolonged pressure during sleep or sitting (e.g., over the deltoid region of the upper arm, the greater trochanter of the femur, or the ischial tuberosity). The more severe lesions healed over several weeks with scarring in some cases. Such lesions should be treated as burns.

Less Common Clinical Trial Adverse Drug Reactions (<1%)

The following reactions occurred in less than 1% of patients: fatigue; body pain; pelvic pain; hypertension; peripheral vascular disease; increased appetite; accelerated growth; anxiety; confusion; paresthesia; thinking abnormalities; vertigo; acne; mechanical irritation at application site; rash at application site; contamination of application site; prostate carcinoma; dysuria; hematuria; impotence; urinary incontinence; urinary tract infection; testicular abnormalities; peripheral edema; gynecomastia; myalgia.

Post-Market Adverse Drug Reactions

In addition to those adverse events reported during clinical trials, the following adverse reactions have been identified during post-marketing use of Androderm and known reactions of testosterone treatment in general. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Table 2: Adverse Drug Reactions from Post-marketing Experience of Androderm and known Adverse Drug Reactions of General Testosterone Treatment:

"CAS Registry No: 58-22-0" System Organ Class (SOC)	Adverse Drug Reaction
Blood and the lymphatic system disorders:	Polycythemia, erythropoiesis abnormal
Cardiovascular disorders:	Tachycardia, atrial fibrillation, pulmonary embolism, and deep vein thrombosis
Endocrine disorders:	Abnormal accelerated growth
Gastrointestinal disorders:	Nausea, vomiting, diarrhea, abdominal pain, gastrointestinal bleeding
General disorders and administration site conditions:	edema, malaise, fatigue, application site burning, application site induration, application site rash, application site dermatitis, application site blister, application site erythema
Hepatobiliary disorders:	Hepatic neoplasms, peliosis hepatis
Immune system disorders:	Allergic reaction, hypersensitivity reaction
Investigations:	Weight increase, fluctuating testosterone levels, testosterone decreased, abnormal liver function tests (e.g. elevated GGTP), lipids abnormalities
Metabolism and nutrition disorders:	Increased appetite, electrolyte changes (nitrogen, potassium, phosphorus, sodium), urine calcium decrease, glucose tolerance impaired, elevated cholesterol
Musculoskeletal and connective tissue disorders:	Myalgia, arthralgia
Nervous system disorders:	Insomnia, headache, dizziness
Psychiatric disorders:	Personality disorder, confusion, anger, aggression, depression, anxiety, decreased libido, cognitive disturbance
Renal and urinary disorders:	dysuria, hematuria, incontinence, bladder irritability
Reproductive system and breast disorders:	Prostrate carcinoma, enlarged prostate (benign), free prostate-specific antigen increased, testicular atrophy, epdidymitis, oligospermia, priapism, impotence, precocious puberty, gynecomastia, mastodynia
Respiratory, thoracic and mediastinal disorders:	Dyspnea, sleep apnea
Skin and subcutaneous tissue disorders:	Pruritus, rash, urticaria, vesiculo-bullous rash, seborrhea, acne, alopecia, male pattern baldness, hirsuitism
Vascular disorders:	Hypertension

DRUG INTERACTIONS

Overview

There are number of potential drug interactions involving testosterone described in the published literature.

No data are available on the interaction with alcohol.

Drug-Drug Interactions

Oxyphenbutazone: Concurrent administration of oxyphenbutazone and androgens may result in elevated serum levels of oxyphenbutazone.

Insulin: In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, insulin requirements.

Propranolol: In a published pharmacokinetic study of an injectable testosterone product, administration of testosterone cypionate led to an increased clearance of propranolol in the majority of men tested. It is unknown if this would apply to Androderm®.

ACTH or Corticosteroids: The concurrent administration of testosterone with ACTH or corticosteroids may enhance edema formation; thus these drugs should be administered cautiously, particularly in patients with cardiac or hepatic disease.

Anticoagulants: Alkylated derivatives of testosterone, such as methandrostenolone, have been reported to decrease the anticoagulant requirement of patients receiving oral anticoagulants. Patients receiving oral anticoagulants therapy require close monitoring, especially when androgens are started or stopped.

Drug-Food Interactions

Interactions with food have not been established.

Drug-Herb Interactions

It was found that some herbal products (e.g. St. John's wort) which are available as over-the-counter (OTC) products might interfere with steroid metabolism and therefore may decrease plasma testosterone levels[10, 11].

Drug-Laboratory Interactions

Androgens may decrease levels of thyroxin-binding globulin, resulting in decreased total T_4 serum levels and increased resin uptake of T_3 and T_4. Free thyroid hormone levels remain unchanged, however, and there is no clinical evidence of thyroid dysfunction.

DOSAGE AND ADMINISTRATION

Dosing Considerations

Measurement of serum testosterone should be repeated taking care to ensure proper patch adhesion and correct time of application before the dose is adjusted. Increasing the daily dose to 7.5 mg (i.e. one 5 mg and one 2.5 mg patch, or three 2.5 mg patches) may be required for men with a higher body weight (>130 kg).

Androderm® therapy for non-virilized patients may be initiated with one 2.5 mg/day patch applied nightly.

The patch should be applied immediately after opening the pouch and removing the protective release liner. The patch should be pressed firmly in place, making sure there is good contact with the skin, especially around the edges.

To ensure proper dosing, the morning serum testosterone concentration may be measured following patch application the previous evening. If the serum concentration is outside the normal range, sampling should be repeated with assurance of proper patch adhesion as well as appropriate application time. Confirmed serum concentrations outside the normal range may require increasing the daily dose to 7.5 mg, i.e. one 5 mg and one 2.5 mg patch, or three 2.5 mg patches, or decreasing the daily dose to 2.5 mg, i.e. one 2.5 mg patch, maintaining nightly application. Because of variability in analytical values among diagnostic laboratories, this laboratory work and any later analyses for assessing the effect of Androderm® therapy, should be performed at the same laboratory so that results can be compared.

Recommended Dose and Dosage Adjustment

The usual starting dose is one Androderm® (testosterone transdermal system) 5 mg or two Androderm® 2.5 mg patches applied nightly (10:00 PM.) and worn for 24 hours, providing a total dose of 5 mg of testosterone/day.

Five (5) mg of testosterone/day (one 5 mg patch or two 2.5 mg patches) is considered the usual maintenance dose for men of normal age/weight range.

A dosage regimen of a single, 5 mg patch or two, 2.5 mg patches should provide serum testosterone levels in the normal range for men of average weight up to 130 kg.

The adhesive side of the Androderm® patch should be applied to a clean, dry area of the skin on the back, abdomen, upper arms, or thighs. Bony prominences, such as the shoulder and hip areas, should be avoided. DO NOT APPLY TO THE SCROTUM. The sites of application should be rotated, with an interval of 7 days between applications to the same site. The area selected should not be oily, damaged, or irritated.

Mild skin irritation can be treated with a topical corticosteroid such as 0.1% triamcinolone acetonide cream[1]. Applying a small amount of 0.1% triamcinolone acetonide cream to the skin under the central drug reservoir of the Androderm® patch has been shown to reduce the incidence and severity of skin irritation. **Ointment formulations should not be used for pretreatment as they may significantly reduce testosterone absorption.**

OVERDOSAGE

Overdosage is not likely due to mode of administration. Serum testosterone has a half life of 70 minutes and therefore falls rapidly once patches are removed.

Oral consumption of the Androderm® patch or the gel contents of the patch will not result in clinically significant serum testosterone concentrations in the target organs due to extensive first-pass metabolism.

No antidote is available. Symptomatic and supportive treatment should be given as indicated by the subject's condition.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Androderm® (testosterone transdermal system) delivers physiologic amounts of testosterone, producing circulating testosterone concentrations that resemble the normal circadian rhythm of healthy young men.

Testosterone

Testosterone, the primary androgenic hormone, is responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics[1]. These effects include the growth and maturation of the prostate, seminal vesicles, penis, and scrotum; development of male hair distribution, such as facial, pubic, chest, and axillary hair; laryngeal enlargement; vocal cord thickening; and alterations in body musculature and fat distribution.

[1] Because of the very small volumes of triamcinolone cream being applied (corresponding to 0.1 mg of the 0.1% topical steroid cream in total per application) it is highly unlikely that drug accumulation will occur. Upon reviewing the safety reports received since this palliative application was approved in the United States, adverse events that would suggest clinically significant drug accumulation or undesirable side effects to this topical steroid application have not been observed. Information on the extent of triamcinolone absorption, absolute bioavailability and disposition is not available.

Male hypogonadism results from insufficient secretion of testosterone and is characterized by low serum testosterone concentrations. Symptoms associated with male hypogonadism include the following: impotence and decreased sexual desire; fatigue and loss of energy; mood depression; regression of secondary sexual characteristics[2].

Pharmacodynamics

Androgens promote retention of nitrogen, sodium, potassium, and phosphorus, and decreased urinary excretion of calcium. Androgens have been reported to increase protein anabolism and decrease protein catabolism. Nitrogen balance is improved only when there is sufficient intake of calories and protein.

Androgens are also responsible for the growth spurt of adolescence and for the eventual termination of linear growth which is brought about by the fusion of the epiphyseal growth centers. In children, exogenous androgens accelerate linear growth rates but may cause disproportionate advancement in bone maturation. Use over long periods may result in fusion of the epiphyseal growth centers and termination of the growth process.

Androgens have been reported to stimulate the production of red blood cells by enhancing erythropoietin production.

During exogenous administration of androgens, endogenous testosterone release is inhibited through feedback inhibition of pituitary LH secretion. With large doses of exogenous androgens, spermatogenesis may also be suppressed through feedback inhibition of pituitary follicle stimulating hormone (FSH) secretion.

Testosterone Transdermal Delivery System

Androderm® (testosterone transdermal system) delivers physiologic amounts of testosterone producing circulating testosterone concentrations that mimic the normal circadian rhythm of healthy young men.

Androderm® is a transdermal patch that provides continuous delivery of testosterone (the primary endogenous androgen) for 24 hours following application to intact, non-scrotal skin (e.g., back, abdomen, thighs, upper arms).

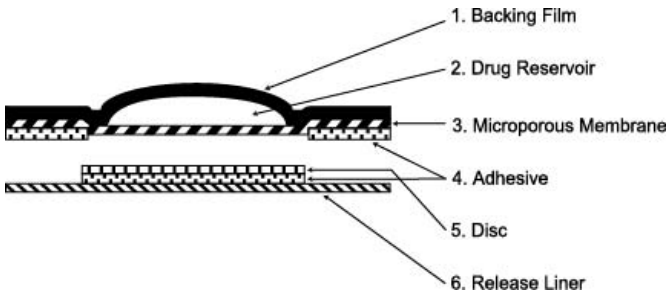
Two strengths of Androderm® are available which deliver *in vivo* 2.5 mg (12.2 mg Transdermal Delivery System) or 5 mg (24.3 mg Transdermal Delivery System) of testosterone per day across skin of average permeability.

Description

Androderm® is a transdermal patch that provides continuous delivery of testosterone (the primary endogenous androgen) for 24 hours following application to intact, non-scrotal skin (e.g. back, abdomen, thighs, upper arm).
Two strengths of Androderm® are available which deliver *in vivo* 2.5 mg or 5 mg of testosterone per day across skin of average permeability.

The Androderm® patch has six components. Proceeding from the top towards the surface attached to the skin, the patch is composed of (1) a metallized polyester/Surlyn®[2] (ethylene-methacrylic acid copolymer)/ethylene vinyl acetate backing film with alcohol resistant ink, (2) a drug reservoir of testosterone USP, alcohol USP, glycerin USP, glyceryl monooleate, and methyl laurate gelled with an acrylic acid copolymer, (3) a permeable polyethylene microporous membrane, and (4) a peripheral layer of acrylic adhesive surrounding the central, active drug delivery area of the patch. Prior to opening of the pack and application to the skin, the central delivery surface of the patch is sealed with a peelable laminate disc (5) composed of a five-layer laminate containing polyester / polyesterurethane adhesive / aluminum foil / polyesterurethane adhesive / polyethylene. The disc is attached to and removed with the release liner (6), a silicone-coated polyester film, which is removed before the patch can be used.

Figure 1



The active ingredient in the patch is testosterone. The remaining components of the patch are pharmacologically inactive.

Pharmacokinetics

Absorption: Following Androderm® (testosterone transdermal system) application to non-scrotal skin, testosterone is continuously absorbed during the 24 hour dosing period. Daily application of two, 2.5 mg patches at approximately 10 PM results in a serum testosterone concentration profile which mimics the normal circadian variation observed in healthy young men (Fig. 2 below). Maximum concentrations occur in the early morning hours with minimum concentrations in the evening.

[2] Surlyn® is a registered trademark of E.I.DuPont de Nemours & Company

Figure 2: Mean (SD) Serum Testosterone Concentrations

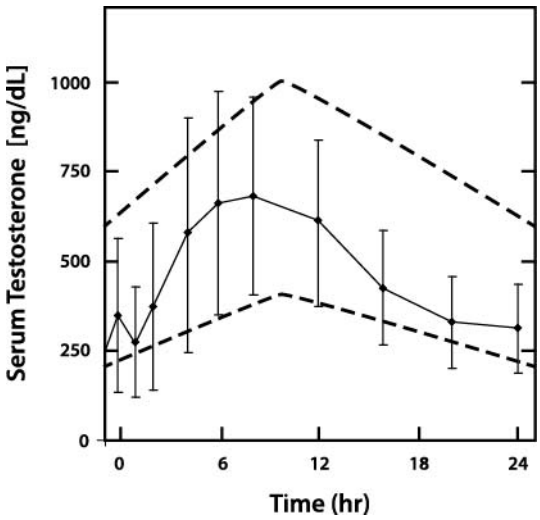


Figure 2: Mean (SD) serum testosterone concentrations during application of Androderm® 2.5 mg patches nightly in 29 hypogonadal male patients; 27 patients used 2 patches nightly and 2 patients used 3 patches nightly. Area between dotted lines shows the 95% confidence interval for the circadian variation observed in healthy young men. Patch application (t=0) was at approximately 10 PM.

In a group of 34 hypogonadal men, application of two, Androderm® 2.5 mg patches to the back, abdomen, thighs, or upper arms resulted in average testosterone absorption of 4 to 5 mg over 24 hours. Applications to the chest and shins resulted in greater inter- individual variability and average 24 hour absorption of 3 to 4 mg. The serum testosterone concentration profiles during application were similar for all sites.

In a steady-state study of 12 hypogonadal men, nightly application of 1, 2, or 3 Androderm® 2.5 mg patches resulted in increases in the mean morning serum testosterone concentrations. These concentrations (including the baseline concentration) averaged 424, 584, and 766 ng/dL with the application of 1, 2 and 3 patches, respectively. The mean baseline serum testosterone concentration was 76 ng/dL.

Normal range morning serum testosterone concentrations are reached during the first day of dosing. There is no accumulation of testosterone during continuous treatment.

In a study of 20 hypogonadal patients, two Androderm® 2.5 mg patches and a single Androderm® 5 mg patch produced equivalent serum testosterone concentration profiles. Average steady-state concentrations over 24 hours were 613±169 and 621±176 ng/dL for the two, 2.5 mg patches and for the single, 5 mg patch, respectively. C_{max} values were 925±340 ng/dL for the two, 2.5 mg patches and 905±254 ng/dL for the single, 5 mg patch.

Distribution: In serum, testosterone is bound with high affinity to sex hormone binding globulin (SHBG) and with low affinity to albumin. The albumin bound portion easily

dissociates and is presumed to be bioactive. The SHBG-bound portion is not considered to be bioactive. The amount of SHBG in serum and the total testosterone concentration determine the distribution of bioactive and non-bioactive androgen.

Bioactive serum testosterone concentrations (BT) measured during Androderm® treatment paralleled the serum testosterone profile (Figure 2) and remained within the normal reference range.

Metabolism: Inactivation of testosterone occurs primarily in the liver. Testosterone is metabolized to various 17-keto steroids through two different pathways, and the major active metabolites are estradiol (E2) and dihydrotestosterone (DHT). DHT binds with greater affinity to SHBG than does testosterone. In reproductive tissues, DHT is further metabolized to 3-alpha and 3-beta androstenediol. (See also reference 6)

In many tissues, the activity of testosterone appears to depend on reduction to dihydrotestosterone (DHT), which binds to cytosol receptor proteins. The steroid-receptor complex is transported to the nucleus, where it initiates transcription events and cellular changes related to androgen action. (See also reference 4)

During steady-state pharmacokinetic studies in 56 hypogonadal men treated with Androderm®, DHT:T and E2:T ratios were comparable to those in normal men, approximately 1:10 and 1:200, respectively.

Upon removal of the Androderm® patches, serum testosterone concentrations decrease with an apparent half-life of approximately 70 minutes. Hypogonadal concentrations are reached within 24 hours following patch removal.

Androderm® therapy suppresses endogenous testosterone secretion via the pituitary/gonadal axis, resulting in a reduction in baseline serum testosterone concentrations compared to the untreated state.

Excretion: Approximately 90% of a testosterone dose given intramuscularly is excreted in the urine as glucuronide and sulfate conjugates of testosterone and its metabolites; about 6% is excreted in the feces, mostly in unconjugated form.

STORAGE AND STABILITY

Androderm® patches should be stored at room temperature (15-30 ˚C), in their sealed pouches until use. Use the patch immediately upon removal from the protective pouch. The reservoir containing the gel may be burst by excessive pressure or heat. Do not use damaged patches. Discard patches in household trash in a manner that prevents accidental application or ingestion by children, pets, or others.

SPECIAL HANDLING INSTRUCTIONS

Discard patches in household trash in a manner that prevents accidental application or ingestion by children, pets, or others.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Androderm® (testosterone transdermal system) 2.5 mg/day
Each patch contains 12.2 mg testosterone for delivery of 2.5 mg of testosterone per day.
Available in cartons of 60 patches.

Androderm® (testosterone transdermal system) 5 mg/day
Each patch contains 24.3 mg testosterone for delivery of 5 mg of testosterone per day. Available in cartons of 30 patches.

Composition:
Androderm® (Testosterone Transdermal System) has a central drug delivery reservoir surrounded by a peripheral adhesive area. The Androderm® 2.5 mg patch has a total contact surface area of 37 cm^2 with a 7.5 cm^2 central drug delivery reservoir containing 12.2 mg testosterone USP, dissolved in an alcohol-based gel. The Androderm® 5 mg patch has a total contact surface area of 44 cm^2 with a 15 cm^2 central drug delivery reservoir containing 24.3 mg testosterone USP, dissolved in an alcohol-based gel. The composition of the gel includes testosterone, alcohol, purified water, glycerin, glycerol monooleate, methyl laurate, carbomer, and sodium hydroxide.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

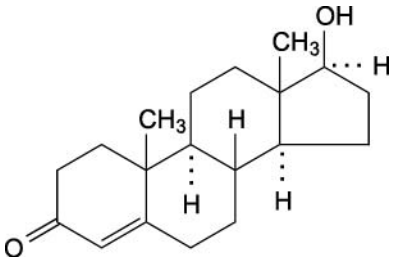
Drug Substance

Proper name: Testosterone

Chemical name: Androst-4-en-3-one, 17-hydroxy, (17ß)-17ß-Hydroxyandrost-4-en-3-one

Molecular formula and molecular mass: $C_{19}H_{28}O_2$

Structural formula:



Testosterone

Molecular Weight: 288.43

Description: Testosterone is a white or creamy white crystalline powder or crystals.

Physicochemical properties: Testosterone has a melting point of 153 - 157°C and gives an optical rotation of +101 - +103° in dioxane. It exhibits strong UV absorption maxima at 238 nm.

When micronized, testosterone is a white or creamy white, crystalline powder. It is odourless, and stable in air. It is only slightly (1%) hygroscopic, soluble in alcohol, acetone, dioxane, chloroform, and other organic solutions. It is practically insoluble in water and only sparingly soluble in vegetable oils.

CAS Registry No: 58-22-0

CLINICAL TRIALS

Study demographics and trial design

In clinical studies using the Androderm® 2.5 mg patch, 93% of patients achieved normal levels of serum testosterone with application of two patches daily, 6% used three daily, and 1% used one patch daily.

The hormonal effects of Androderm® as a treatment for male hypogonadism were demonstrated in four open-label trials that included 94 hypogonadal men, ages 15 to 65 years. In these trials, Androderm® produced average morning serum testosterone concentrations within the normal reference range in 92% of patients. The mean (SD) serum hormone concentrations and percentage of patients who achieved average concentrations within the normal ranges are shown in Table 1 below.

Table 1: Individual morning serum hormone concentrations (ng/dL) and percent of patients with mean concentrations within the normal range during continuous Androderm® treatment (n=94).

	T	BT	DHT	E2
Normal Range*	(306-1031)	(93-420)	(28-85)	(0.9-3.6)
Mean	589	312	47	2.7
SD	209	127	18	1.2
% Normal	92	88	85	77
% High	1	12	2	22
% Low	7	0	13	1

Abbreviations: T = testosterone, BT = bioavailable testosterone,
DHT = dihydrotestosterone, E2 = estradiol
* Lower number is the 2.5 percentile, higher number the 97.5 percentile.
Source: Endocrine Sciences (1991).

A physiological suppression of the pituitary/gonadal axis occurs during continuous Androderm® treatment, leading to reduced serum LH concentrations. In clinical trials, 10 out of 21 men (48%) with primary (hypergonadotropic) hypogonadism achieved normal range LH concentrations within 6-12 months of treatment. LH concentrations may remain elevated in some patients despite serum testosterone concentrations within the normal range.

Comparison with intramuscular testosterone: Sixty-six patients, previously treated with testosterone injections, received Androderm® or intramuscular testosterone enanthate (200 mg every 2 weeks) treatment for 6 months. The percent of time that serum concentrations remained within the normal range (throughout the dosing interval) were as follows (Table 2):

Table 2: Comparison of percent of patients receiving Androderm® or intramuscular testosterone with serum concentrations within the normal range.

	T	BT	DHT	E2
ANDRODERM®	82%	87%	76%	81%
IM	72%	39%	70%	35%
p value	0.05	< 0.001	0.06	< 0.001

Sexual function was comparable between groups.

DETAILED PHARMACOLOGY

Following Androderm® (testosterone transdermal system) application to non-scrotal skin, testosterone is continuously absorbed during the 24 hour dosing period. Daily application of two, 2.5 mg patches at approximately 10 PM results in a serum testosterone concentration profile which mimics the normal circadian variation observed in healthy young men (Fig. 2 below). Maximum concentrations occur in the early morning hours with minimum concentrations in the evening.

Figure 2: Mean (SD) Serum Testosterone Concentrations

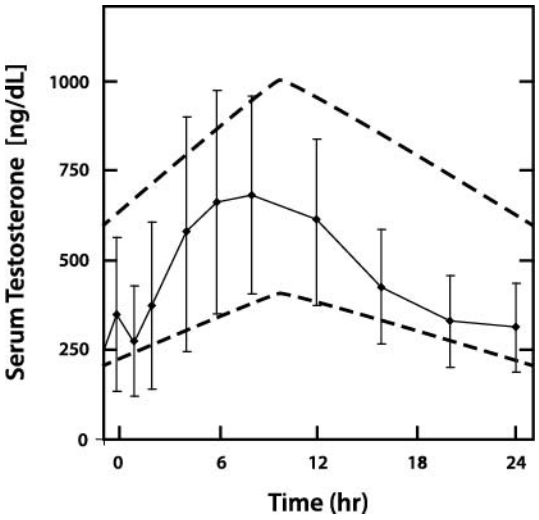


Figure 2: Mean (SD) serum testosterone concentrations during application of Androderm® 2.5 mg patches nightly in 29 hypogonadal male patients; 27 patients used 2 patches nightly and 2 patients used 3 patches nightly. Area between dotted lines shows the 95% confidence interval for the circadian variation observed in healthy young men. Patch application (t=0) was at approximately 10 PM.

In a group of 34 hypogonadal men, application of two, Androderm® 2.5 mg patches to the back, abdomen, thighs, or upper arms resulted in average testosterone absorption of 4 to 5 mg over 24 hours. Applications to the chest and shins resulted in greater inter- individual variability and

average 24 hour absorption of 3 to 4 mg. The serum testosterone concentration profiles during application were similar for all sites.

In a steady-state study of 12 hypogonadal men, nightly application of 1, 2, or 3 Androderm® 2.5 mg patches resulted in increases in the mean morning serum testosterone concentrations. These concentrations (including the baseline concentration) averaged 424, 584, and 766 ng/dL with the application of 1, 2 and 3 patches, respectively. The mean baseline serum testosterone concentration was 76 ng/dL.

Normal range morning serum testosterone concentrations are reached during the first day of dosing. There is no accumulation of testosterone during continuous treatment.

In a study of 20 hypogonadal patients, two Androderm® 2.5 mg patches and a single Androderm® 5 mg patch produced equivalent serum testosterone concentration profiles. Average steady-state concentrations over 24 hours were 613±169 and 621±176 ng/dL for the two, 2.5 mg patches and for the single, 5 mg patch, respectively. C_{max} values were 925±340 ng/dL for the two, 2.5 mg patches and 905±254 ng/dL for the single, 5 mg patch.

Upon removal of the Androderm® patches, serum testosterone concentrations decrease with an apparent half-life of approximately 70 minutes. Hypogonadal concentrations are reached within 24 hours following patch removal.

Androderm® therapy suppresses endogenous testosterone secretion via the pituitary/gonadal axis, resulting in a reduction in baseline serum testosterone concentrations compared to the untreated state.

In serum, testosterone is bound with high affinity to sex hormone binding globulin (SHBG) and with low affinity to albumin. The albumin bound portion easily dissociates and is presumed to be bioactive. The SHBG-bound portion is not considered to be bioactive. The amount of SHBG in serum and the total testosterone concentration determine the distribution of bioactive and non-bioactive androgen.

Bioactive serum testosterone concentrations (BT) measured during Androderm® treatment paralleled the serum testosterone profile (Figure 2) and remained within the normal reference range.
Approximately 90% of a testosterone dose given intramuscularly is excreted in the urine as glucuronide and sulfate conjugates of testosterone and its metabolites; about 6% is excreted in the feces, mostly in unconjugated form. Inactivation of testosterone occurs primarily in the liver. Testosterone is metabolized to various 17-keto steroids through two different pathways, and the major active metabolites are estradiol (E2) and dihydrotestosterone (DHT). DHT binds with greater affinity to SHBG than does testosterone. In reproductive tissues, DHT is further metabolized to 3-alpha and 3-beta androstenediol. (See also reference 6)

During steady-state pharmacokinetic studies in 56 hypogonadal men treated with Androderm®, DHT:T and E2:T ratios were comparable to those in normal men, approximately 1:10 and 1:200, respectively.

In many tissues, the activity of testosterone appears to depend on reduction to dihydrotestosterone (DHT), which binds to cytosol receptor proteins. The steroid-receptor complex is transported to the nucleus, where it initiates transcription events and cellular changes related to androgen action. (See also reference 4)

TOXICOLOGY

The toxicology of testosterone has been summarized for various animal species and for humans in the following publications:

- National Institute for Occupational Safety and Health RTECS, April 1989 (RTECS no. XA3030000)
- Shepard, Thomas H., Catalog of Teratogenic Agents, 6th Edition, Johns Hopkins University Press, (p.1755) (1989)
- IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, vol. 21 (pp.209-217 and 519-547) (1979)

REFERENCES

1. Rommerts FFG. Testosterone: an overview of biosynthesis, transport, metabolism and action in Nieschlag E, Behre HM eds. Testosterone Action Deficiency and Substitution, 1990 Springer-Verlag, Berlin p.1022

2. Santen RJ. Chapter 21: Male hypogonadism in Yen SSC and Jaffe RB eds., Reproductive Endocrinology, 3rd Edition, 1991 WB Saunders Company, Philadelphia PA, 739-794

3. Allan, C.A. and McLachlan, R.I. (2004): Age-related changes in testosterone and the role of replacement therapy in older men. Clin. Endocrinol. 60, (6), 653-670

4. Nieschlag, E. and Behre, H.M. (Editors): Testosterone: Action, Deficiency, Substitution. 3rd edition, Cambridge University Press, (2004)

5. Rhoden, E.L. and Morgentaler, A. (2004): Risks of testosterone-replacement therapy and recommendations for monitoring. N. Engl. J. Med. 350, 482-492

6. Wang, C., Catlin, D.H., Starcevic, B. et al. (2004): Testosterone metabolic clearance and production rates determined by stable isotope dilution/tandem mass spectrometry in normal men: Influence of ethnicity and age. J. Clin. Endocrinol. Metab., 89, (6), 2936-2941

7. Wilson, D.E., Kaldbey, K., Boike, S.C. and Jorkasky, D.K. (1998): Use of topical corticosteroid pretreatment to reduce the incidence and severity of skin reactions associated with testosterone transdermal therapy. Clinical therapeutics, 20, 299-306

8. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS et al. Testosterone therapy in adult men with androgen deficiency syndromes: An endocrine society clinical practice guideline. J Clin Endocrinol Metab 2006;91(6):1995-2010.

9. Medras M, Filus A, Jozkow P, Winowski J, Sicinska-Werner T. (2006) Breast cancer and long-term hormonal treatment of male hypogonadism. Breast Cancer Research and Treatment 96:263-265.

10. Markowitz JS, Donovan JL, DeVane CL, Taylor RM, Ruan Y, Wang J, Chavin KD. (2003) Effect of St John's Wort on drug metabolism by induction of cytochrome P450 3A4 enzyme. JAMA 290(11):1500-1504.

11. Donovan JL, DeVane CL, Lewis JG, Wang J, Ruan Y, Chavin KD, Markowitz JS. (2005) Effects of St John's Wort (Hypericum perforatum L.) extract on plasma androgen concentrations in healthy men and women: A pilot study. Phytotherapy Research 19:901-906.

PART III: CONSUMER INFORMATION
ANDRODERM®

Testosterone Transdermal Delivery System

This leaflet is part III of a three-part "Product Monograph" published when Androderm® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Androderm®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
Your doctor has prescribed this medicine because your body is not making enough testosterone. The medical term for this condition is hypogonadism.

What it does:
Androderm® delivers medicine into your bloodstream through your skin. Androderm® helps raise your testosterone to normal levels.

When it should not be used:

- If you have or it is suspected that you have prostate or breast cancer.
- If you have difficulty in urinating due to an enlarged prostate
- Known allergy to any of its components [the active ingredient is testosterone, which may be synthesized from soy; (see "What the nonmedicinal ingredients are" in this section)]

Androderm® should NOT be used by women. Pregnant and breast feeding women are especially at risk and should avoid skin contact with application sites on men. Testosterone may cause harm to your unborn baby.

What the medicinal ingredient is:
Testosterone USP.

What the nonmedicinal ingredients are:
Alcohol, carbomer, glycerin, glycerol monooleate, methyl laurate, purified water and sodium hydroxide.

What dosage forms it comes in:
Androderm® (testosterone transdermal system) **2.5 mg/day**
Each patch contains 12.2 mg testosterone for delivery of 2.5 mg of testosterone per day. Available in cartons of 60 patches.

Androderm® (testosterone transdermal system)
5 mg/day
Each patch contains 24.3 mg testosterone for delivery of 5 mg of testosterone per day. Available in cartons of 30 patches.

WARNINGS AND PRECAUTIONS

Androderm is not indicated for use in children < 18 years of age

There is very little information from clinical trials with testosterone in the older male (>65 years of age) to support safe use for a long period of time.

You should not use testosterone in an attempt to reduce weight and increase muscle, or improve athletic performance as it may cause serious health problems.

You should not use testosterone to treat sexual dysfunction or male infertility.

Before using Androderm®, talk to your doctor if you:

- Have heart or blood vessel problems or a history of these problems such as heart attacks, stroke, or blood clot in the lungs or the legs
- have difficulty urinating due to an enlarged prostate. Older patients may have a higher risk of developing an enlarged prostate or prostate cancer;
- have prostate cancer (confirmed or suspected);
- have liver, kidney or heart disease;
- have high blood pressure (hypertension);
- have diabetes
- have breathing problems during sleep (sleep apnea).

Skin burns have been reported at the patch site in patients wearing an aluminised transdermal system during a magnetic

resonance image scan (MRI). Because Androderm contains aluminium it is recommended to remove the system before undergoing an MRI.

Drug Abuse and Dependence:
Androderm® contains testosterone, which is a controlled substance under Schedule G of the Food and Drugs Act.

Precautions while using Androderm®
Androderm® can be transferred to another person, including children, when skin-to-skin contact is made with the application sites.

You should prevent Androderm® from transferring to another person, especially pregnant or breast feeding women, or children by taking the following precautions:

- Wash hands immediately with soap and water after application of Androderm®:

In the event that an unwashed or uncovered Androderm® application site does come in direct contact with the skin of another person, the general area of contact on the other person should be washed with soap and water as soon as possible.

Changes in body hair distribution, significant increase in acne, or other signs of the development of masculine traits in the female partner or in any person (including children) exposed to skin-to-skin contact, should be brought to the attention of a doctor.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or pharmacist if you are taking or have recently taken any other drugs or herbal products, even those without a prescription.

Drugs that may interact with Androderm® include:
- Insulin
- Corticosteroids
- Propranolol
- Warfarin

PROPER USE OF THIS MEDICATION

It is essential that you take Androderm exactly as your doctor has prescribed, and follow the following recommendations regarding use of the patches.

Recommendations on When and Where to Apply Androderm®

1. Apply one 5 mg or two 2.5 mg patches which will deliver 5 mg of testosterone per day into the body.

2. Apply the patch at night (around 10:00 PM). Nightly application results in a daily variation of circulating testosterone levels similar to the pattern in healthy young men.

3. Apply the patch to clean dry areas of the body, such as back, abdomen, thighs, and upper arms (see figure 4). Only apply the patch to healthy, normal skin.

4. Never apply the patch to the scrotum, mucosal surface (i.e. inside of mouth or nose), or damaged skin (open sores, wound, irritation, sun burn).

5. Avoid application of the patch to bony areas, such as the point of shoulder and the upper hip or on a part of the body that could be subjected to prolonged pressure during sleep or sitting. Application to these sites has been associated with burn-like blisters. Skin areas which are oily, perspire intensely or are covered with hair may interfere with adhesion of the patches and should be avoided.

6. Change the patch every 24 hours. The new patch should never be applied to the places just used.

7. Rotate application sites regularly: to prevent irritation, do not reapply patches to a previously used area for at least 7 days. If you experience skin irritation talk to

your pharmacist or doctor.

8. Maintain normal activities: When applied to clean dry skin, the patch will remain in place during normal activities. Currently it is unknown how long showering or swimming should be delayed after application of Androderm. Androderm® does not have to be removed during sexual intercourse. Androderm® does not have to be removed while bathing.

9. What to do if the patches falls off: If a patch falls off, do not replace it until the night time application (when a new site should be chosen). If a patch becomes loose, smooth it down again by rubbing over the perimeter of the patch.

10. What to do if Androderm gets in the eye: if you get Androderm in your eyes, rinse your eyes right away with warm, clean water to flush out any Androderm. Call your doctor if discomfort persists.

11. What to do if you miss a dose of Androderm®:
if you miss a dose, do not double your next dose the next day to catch up. Resume your normal dosing the next day.

Androderm® should be used with caution by men with previous history of photosensitivity or hypersensitivity to topically applied medications, and by those individuals who have been sun burnt in the area of the proposed application site within three weeks prior to the initiation of treatment.

How to apply the patch

After choosing an application site according to the above recommendations, apply Androderm® patch as follows:

1. Open the Pouch: Open the pouch containing the Androderm® patch by tearing along the edge (Figure 1). Remove the patch from the pouch.

Figure 1

2. Prepare the Patch for Application: Grasp the tabs on the patch and protective plastic liner (Figure 2). While firmly holding the clear plastic liner, gently pull open, exposing the adhesive and central reservoir area
(Figure 3). Discard the liner.

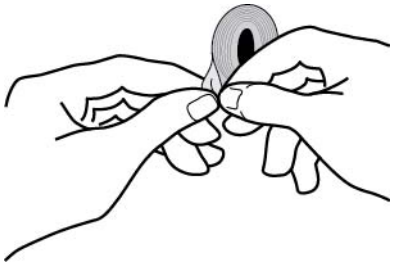


Figure 2

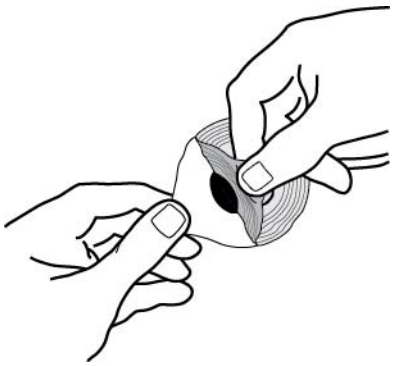
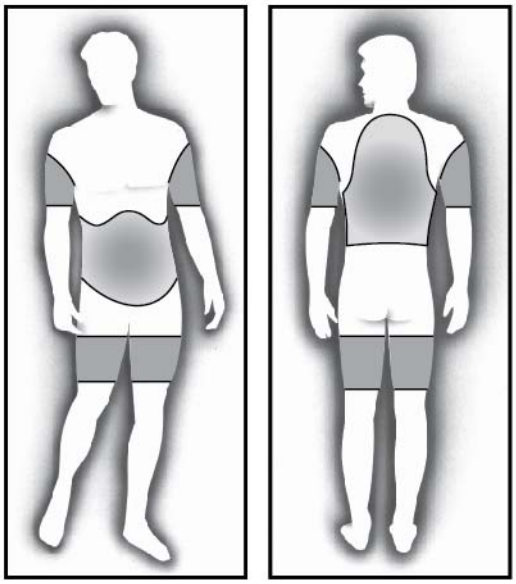


Figure 3

3. Apply the Patch: Place the patch on the skin and firmly press around the edges to insure that the patch adheres to the skin. The patch must lie flat against the skin to insure proper testosterone absorption. The best areas to apply patches are: the back, abdomen, thighs and upper arms (see Figure 4).

Figure 4



Front **Back**

Overdose:
If you use more Androderm than the recommended dose, wash the skin with soap and water where Androderm was applied and contact your doctor or pharmacist.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, Androderm® can have side effects. The following side effects have been reported for products containing testosterone:

- Increased or irregular heart rate, blood clot in the lungs or the legs
- skin irritation or redness or rash at the application site;
- increased prostatic specific antigen (PSA);
- enlarged prostate (benign prostatic hyperplasia);
- an increase in red blood cell count, (hematocrit and hemoglobin);
- acne;
- change in mood, depression;
- prolonged or painful erection;
- sleep disturbances caused by breathing problems;
- aggression or aggressive behaviour;
- breast enlargement and breast pain;
- loss of hair and baldness;
- high blood pressure
- weight gain;
- headache, dizziness.

Please talk to your doctor if your female partner develops changes in hair distribution, increases in acne, or signs of masculinity.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/ Effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Urinary symptoms (i.e. change in frequency / color, dribbling, pain on urination straining, weak stream, small amounts)		√	
Uncommon (after prolonged use)	Breast enlargement or breast pain		√	
Uncommon	Heart attack and stroke			√
Uncommon	Swelling of ankles and legs (in patients with heart, kidney or liver damage)			√
Uncommon	Erections that are too frequent or continue for too long, or are painful.		√	
Uncommon	Liver problems, with symptoms such as nausea, vomiting, along with yellowed or darkened skin			√

This is not a complete list of side effects. For any unexpected effects while taking Androderm®, contact your doctor or pharmacist.

HOW TO STORE IT

Store Androderm® at room temperature (15°C-30°C).

Keep in a safe place out of reach of children and pets.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at www.allergan.ca or by contacting Allergan Inc. at 1-800-668-6424.

This leaflet was prepared by:
Allergan Inc.
Markham, Ontario L6G 0B5
CANADA

Date of preparation: February 28, 2018

ANDRODERM® is a registered trademark of Allergan Sales, LLC, used under license by Allergan Inc.