

## PRODUCT INFORMATION

### Description

ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream is a transdermal drug delivery system consisting of a white vanishing cream intended for scrotal administration.

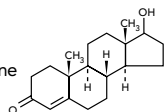
ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream contains dl-α-tocopherol acetate (vitamin E), almond oil and macadamia nut oil formulated to optimize systemic absorption of the active ingredient. Also contains cetomacrogol 1000, cetostearyl alcohol, butylated hydroxytoluene, propyl hydroxybenzoate, anhydrous citric acid, methyl hydroxybenzoate, triethanolamine, carbomer 940, B & J Phenonip<sup>®</sup> and purified water.

### Chemical Structure

Testosterone.

17-β-Hydroxyandrost-4-en-3-one

C<sub>19</sub>H<sub>28</sub>O<sub>2</sub> = 288.4.



Testosterone is a white crystalline powder, or colorless or yellowish-white crystals, practically insoluble in water, freely soluble in alcohol and in methylene chloride, practically insoluble in fatty oils. CAS- 58-22-0.

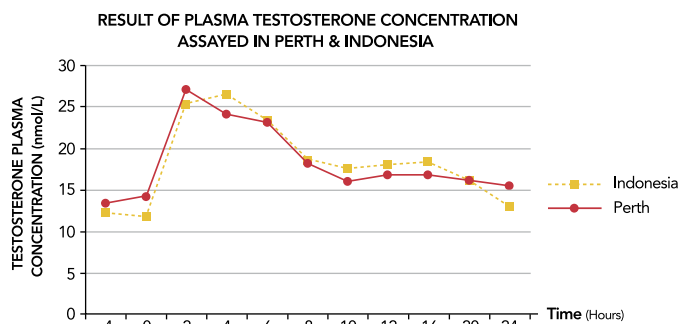
### Pharmacology

Testosterone is the primary androgenic hormone. Testosterone is produced by the interstitial (Leydig) cells of the testes and the adrenal glands in males and by the ovary and adrenal glands in females. Testosterone is responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. Secondary sex characteristics include growth and maturation of the prostate, seminal vesicles, penis and scrotum; male hair distribution, deepening of the voice, changes in fat distribution and muscle mass.

### Pharmacokinetics

The majority of testosterone produced (98-99%) is biologically inactive due to binding to sex hormone-binding globulin (SHBG) and albumin (55% and 45% respectively to the bound portion). Testosterone also circulates unbound as a free hormone (1-2%) and is considered biologically active. Testosterone is metabolized primarily in the liver and also in peripheral tissue. Dihydrotestosterone (DHT) and oestradiol (E2) are products of testosterone metabolism. DHT is produced by reduction through the action of the enzyme 5-α reductase, which is present in genital tissue, skin and the prostate. DHT is further metabolized to 3-α and 3-β androstane diol. DHT binds with greater affinity to SHBG than does testosterone. E2 is produced by aromatisation of testosterone. DHT: testosterone and E2: testosterone ratios in normal adult males are 1:10 and 1:200 respectively. 90% of testosterone is excreted in the urine as glucuronide and sulphate conjugates of testosterone and its metabolites. Scrotal skin is up to 42 times more receptive to the absorption of steroids than other sites of application including the back, axilla and forearms<sup>1</sup>. Daily application of ANDROMEN<sup>®</sup> FORTE to the scrotum results in a serum testosterone concentration profile within the normal range observed in healthy young men. Maximum serum testosterone concentration occurs 3-5 hours after application as shown in Figure 1.

Fig. 1 Mean (SD) plasma testosterone concentrations using 50mg testosterone (2 units) scrotally once daily application of ANDROMEN<sup>®</sup> FORTE in 8 hypogonadal males.



Normal range serum testosterone concentrations (10-35nmol/L) are reached during the first day of dosing using a 50mg single dose applied to the scrotum. There is no accumulation of testosterone during continuous treatment. A steady-state level is achieved within 10 days of initiating therapy. A single daily application of 1-2 units of cream (25-50mg testosterone) of ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream to the scrotum results in a serum concentration profile within the normal therapeutic range for healthy young males.

### Indications

ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream is indicated for testosterone replacement therapy for symptomatic testosterone deficient males, including confirmed primary hypogonadism, secondary hypogonadism and late-onset hypogonadism.

### Contra Indications

Testosterone is contraindicated in men with known or suspected carcinoma of the prostate, known or suspected carcinoma of the breast, known or suspected androgen dependent neoplasia, nephrotic syndrome or hypercalcaemia.

Known sensitivity to testosterone, ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream or any of its components.

ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream contains almond oil and macadamia nut oil. ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream has not been evaluated in women and is contraindicated in pregnancy and while lactating.

The product is not suitable for children.

### Precautions

**EXTREMELY IMPORTANT:** Before initiating ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream treatment surveillance for prostate cancer by means of digital rectal examination (DRE) and a blood test for Prostate-Specific Antigen (PSA) is recommended. Caution is warranted if the PSA is normal-high because in hypogonadal patients the PSA is generally inappropriately low. Furthermore a post treatment increase in PSA more than the normal range should raise suspicion about prostate disease. International guidelines recommend reviewing PSA each 3 months for the first 12 months then each 12 months thereafter. If there is a 1.5 increase of PSA during a 12 month period further evaluation is required even if under age related normal cut-off. Hemoglobin and hematocrit should be checked periodically to detect polycythemia in patients receiving androgen therapy. Liver function, PSA, total and HDL cholesterol should also be monitored. Patients with pre-existing cardiac, hepatic or renal diseases need to be monitored closely when undergoing androgen treatment. High level athletes need to be aware of the rules governing androgen use if prescribed ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream. Androgen supplementation in geriatric patients may increase the risk for the development of prostatic hyperplasia.

### Paediatric Use

This product is not suitable for children. Care should be taken to ensure that children do not come into contact with ANDROMEN<sup>®</sup> FORTE application sites. In the event of contact, wash with soap and water as soon as possible.

### Adverse Reactions

Potential side effects from excessive dosing may include:

- Nausea, vomiting, jaundice or swelling of the ankles
- Increased body hair
- Increased acne
- Signs of virilization
- Weight gain
- Persistent headaches
- Increased appetite
- Deepening of the voice
- Electrolyte disturbances
- Too frequent or persistent erections of the penis (priapism)
- Gynecomastia

Whilst none of these effects has been reported with ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream, either in trials or clinical use, they may potentially occur with excessive prolonged testosterone usage.

Patients should be made aware of the consequences of making **sustained long-term close physical contact** with young children and partners. There is the potential for passive transfer of testosterone from the area of application to the skin of individuals with who close contact is made. Long term continual exposure may result in passive absorption and may have adverse effects, including virilization, in young children.

### Dosage and Administration

Administration via scrotal application provides a convenient acceptable mode of administration. ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream is absorbed from skin sites other than the scrotum including torso, back, chest, arm and legs however absorption may be variable and is not as complete as via scrotal application. If these other skin sites are to be used the dose may need to be significantly increased to achieve comparable serum testosterone levels as for scrotal application.

ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream is supplied with a dose measuring applicator.

The appropriate dose is achieved by directing the patient to apply a defined amount of cream to the scrotum and massaging until vanished.

The scrotum is not required to be shaved prior to use. Absorption is likely to be less complete and variable if applied to other areas of the body and therefore administration should be solely to the scrotum.

### Dosage

ANDROMEN<sup>®</sup> FORTE 5% testosterone cream contains 50mg testosterone BP per 1gm via the applicator. A baseline total serum testosterone level, sex-hormone binding globulin (SHBG) or free testosterone should be measured before initiating treatment.

Recommended starting dose is 50mg testosterone (2 units on the applicator) of cream applied once daily and massaged into the scrotum until the cream is absorbed (usually 30-60 seconds). Dose is variable according to severity of symptoms and clinical response.

Variations may occur between plasma levels achieved and their time course between different individuals.

Clinical response is usually observed 3-4 weeks after initiation of treatment where upon dose may be reduced to maintenance if desired.

ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream should be applied to clean dry scrotal skin.

There is no necessity to shave or removal hair from scrotum prior to use.

ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream should be applied immediately after being dispensed from the tube.

ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream is only recommended for use in men.

### Use in Pregnancy

Category D. Testosterone is suspected to cause birth defects when administered during pregnancy. ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream has not been evaluated in women and is contraindicated during pregnancy. See Contraindications.

### Use in Lactation

Testosterone will suppress prolactin in the lactating female and may cause adverse effects in the infant. ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream has not been evaluated in women and should not be used in breast-feeding women. See Contraindications.

### Overdose

This is not likely due to the mode of administration. Blood testing of serum testosterone levels should be undertaken within one month of initiating therapy to monitor therapy. If serum testosterone levels are raised beyond the therapeutic normal range the dose can be adjusted downwards. Serum testosterone levels fall to baseline levels within 72 hours of ceasing treatment.

### Presentation

ANDROMEN<sup>®</sup> FORTE 5% testosterone cream containing 50mg/g testosterone BP in a 50g boxed tube. ANDROMEN<sup>®</sup> FORTE 5% w/w testosterone cream is supplied with a dose applicator calibrated in 1 unit graduations. One unit approximates to 0.5 gm of cream (25mg testosterone). The patient should measure the appropriate dose using the applicator and apply directly to the scrotal skin massaging until absorbed.

### Storage

Store below 25°C. DO NOT FREEZE  
Shelf-life under these conditions is three years.  
POISONS SCHEDULE S4 Prescription only

### Name and Address of Sponsor

Lawley Pharmaceuticals  
61 Walcott Street, Mt Lawley Perth, WA 6050 Australia  
ABN 33 890 156 936

### Postal Address

P.O. Box 448, Mt. Lawley, Perth, WA 6050, Australia  
Telephone: +61 8 9228 9033  
Fax: +61 8 9228 9455  
Website: www.lawleypharm.com.au  
Email: info@lawleypharm.com.au  
AUST L 95334  
Date of Preparation: November 2007

Ref: 1. Feldmann RJ, Maibach HI. Regional variation in percutaneous penetration of 14C cortisol in man. J Invest Dermatol. 1967;48:181-3.