PRODUCT INFORMATION

Composition
- Active: Testosterone B.P.
- Chemical Structure: 17β-Hydroxyandrost-4-en-3-one
- Molecular Weight: 288.4
- CAS: 58-22-0

Description
ANDROFEME® 1% w/v testosterone cream is a transdermal drug delivery system consisting of a white vanishing cream intended for use in women. ANDROFEME® 1% w/v testosterone cream contains α-tocopherol acetate (vitamin E) and almond oil formulated to optimise systemic absorption of the active ingredient. Also contains cetomacrocol 1000, cetostearyl alcohol, butylated hydroxytoluene, anhydrous citric acid, triethanolamine, carbon 940, B & J Phenonip® and purified water.

Indication
ANDROFEME® is indicated for the management of symptoms associated with low testosterone in women. Symptoms most commonly include reduced sexual motivation, loss of desire and overall diminished sexual satisfaction.

Pharmacology
Testosterone is the primary androgenic hormone. Testosterone and its 5α-reduced metabolite dihydrotestosterone (DHT) activate the intracellular androgen receptor and modulate gene transcription. Testosterone is produced in the adrenal glands and the ovaries in females. In males, testosterone is responsible for the normal growth and development of the male sex organs and for maintenance of secondary characteristics. In women androgens act directly via the androgen receptors in tissues, such as bone, skin fibroblasts, hair follicles and sebaceous glands. Testosterone is a precursor hormone for estrogen biosynthesis in the ovaries and at extragonadal sites - bone, brain, cardiovascular and adipose tissues. Testosterone exerts a strong influence on female sexuality and has a physiological role in bone development and maintenance of mineralisation.

Pharmacokinetics
The majority of testosterone binds to sex hormone-binding globulin (SHBG) and is biologically inactive. Testosterone also circulates unbound as a free hormone and is considered biologically active. Testosterone is metabolized primarily in the liver and also in peripheral tissue. Dihydrotestosterone (DHT) and estradiol (E2) are products of testosterone metabolism. DHT is produced by reduction through the action of the enzyme 5α-reductase, which is present in genital tissue and skin. DHT is further metabolized to 3α-alpha and 3-beta androstanediol. DHT binds with greater affinity to SHBG than does testosterone. E2 is produced by aromatisation of testosterone. 90% of testosterone is excreted in the urine as glucuronide and sulphate conjugates of testosterone and its metabolites.

Following ANDROFEME® application to the skin, serum testosterone begins to rise within an hour of application. A steady-state level is achieved within 2 weeks of initiating therapy. A single daily application of 1ml via measured applicator (10mg testosterone) of ANDROFEME® to the inner aspects of the forearm results in a serum concentration profile in the upper range to that observed in healthy young females.

Precautions
Androgen supplementation in women must be monitored closely, especially at onset of treatment. Female requirements for testosterone are between ten and twenty times less than that of males. Normal ranges for testosterone may vary between laboratories and between different assay methods. Supraphysiological levels may be achieved if doses are too high, therefore individual assessment and monitoring needs to be implemented on a patient-by-patient basis. If high levels are achieved treatment should be halted and recommenced after reduced levels have been established. Levels typically return to baseline 2-5 days after ceasing treatment. All patients with pre-existing cardiac, hepatic or renal diseases need to be monitored closely when undergoing androgen treatment. ANDROFEME® testosterone therapy is contraindicated in women with normal reproductive function because of the potential for virilisation of a female fetus unless adequate contraceptive measures are being utilised.

Use in Pregnancy
Category D. ANDROFEME® is not to be used in pregnant women under any circumstance. Testosterone is known to have the potential to cause serious birth defects when administered during pregnancy. (See Contraindications)

Use in Lactation
Testosterone suppresses prolactin in the lactating female and may cause adverse effects in the infant. ANDROFEME® must not be used in breast-feeding women. (see Contraindications)

Care should be taken by breast-feeding women to avoid any contact with ANDROFEME®. In the event of contact, wash with soap and water as soon as possible.

Paediatric Use
This product is not suitable for children. Care should be taken to ensure that children do not come into contact with ANDROFEME® application sites. In the event of contact, wash with soap and water as soon as possible.

Adverse Reactions
ANDROFEME® is characterised by its significant lack of side effects in clinical use. No skin irritation has been reported at the sites of application. Potential side effects from excessive dosing may include:
- Nausea, vomiting, jaundice or swelling of the ankles
- Increased body hair
- Signs of virilization
- Weight gain
- Persistent headaches
- Deepening of the voice
- Electrolyte disturbances
- Polycythemia

Whilst none of these effects have been reported with ANDROFEME®, either in trials or clinical use, they are a potential side effect from excessive prolonged testosterone usage.

In women, the inhibitory action of androgens on the activity of the anterior pituitary may result in the suppression of ovarian activity and menstruation. Continued administration of large doses may produce symptoms of virilism, such as male-pattern hirsutism or baldness, deepening of the voice, atrophy of the breasts and endometrial tissue, oily skin, acne, hypertrophy of the clitoris and suppression of lactation.

Patients should contact their doctor if any of the above should occur.

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

Indication
ANDROFEME® is indicated for testosterone deficiency in females.
PRODUCT INFORMATION (cont’d)

Dosage and Administration

Prior to prescribing:

Topical application provides a convenient and acceptable delivery method for administering testosterone to women. Clinical manifestations of testosterone deficiency in testosterone deficient women differ vastly in individuals and may be present in tandem with other clinical disorders. The following flowchart* provides a management algorithm to assist in making a diagnosis prior to initiating therapy.

If the patient meets the above criteria, counselling as to the benefits and potential risks of androgen therapy should be provided, including discussions on the lack of data on the safety of long-term use.

If the patient consents to initiating testosterone therapy careful monitoring should be provided for the initial three months of treatment and an evaluation of treatment be undertaken at the conclusion of the third month. Testing at this time should include monitoring of the liver function, haemoglobin and lipids. A full evaluation of the treatment be undertaken at the conclusion of the third month.

Clinical trials have shown that there is a four to eight week time lag between starting testosterone treatment and an improvement in sexual motivation. If there is no improvement in symptoms after 6 months of continuous therapy then alternative treatments should be considered.

The usual starting dose of ANDROFEME® is 5mg testosterone (0.5mL of cream via applicator) applied once daily to the inner aspects of either the lower torso or upper outer thigh. Absorption may be more variable if applied to other areas of the body. The dose can be varied according to severity of symptoms and clinical response.

The patient should have a follow-up blood test taken within three weeks of initiating treatment. Levels should be maintained at the upper end of the normal therapeutic range for females. The dose should be titrated as deemed appropriate. Follow-up should occur at 4 weeks and a full evaluation of the treatment be undertaken at the conclusion of the third month.

Do not apply to the genitalia or perineum, unless required for a specified purpose.

Women should be made aware prior to initiating testosterone treatment of the lack of long term safety data associated with testosterone use in women. Treatment with ANDROFEME® should be on a short term basis – 3 months with regular monitoring (see Directions for use) – and it is at the physician’s discretion if treatment is to be continued.

Caution should be exercised when patients are taking products that may decrease sex hormone-binding globulin (SHBG) or increase free-testosterone levels.

Overdose

This is not likely due to the mode of administration.

Presentation

ANDROFEME® 1% cream containing 10mg/mL testosterone BP in a 50mL boxed tube.

ANDROFEME® is supplied with a dose applicator marked with 0.5mL graduations. Each 0.5mL delivers a 5mg dose of testosterone. The patient should be directed to measure the appropriate dose using the graduated applicator and then apply to the skin. ANDROFEME® should be applied to clean dry skin.

Storage

Store below 25°C. DO NOT FREEZE.

Shelf-life under these conditions is two years.

Store at 15°C to 30°C for 2 years. After opening, store as directed on the label. When no further use of the product is anticipated, the remaining contents of the tube should be disposed of.

Name and Address of Supplier

Distributed by Lawley Pharmaceuticals Pty Ltd for Lawley Pharmaceuticals

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ANDROFEME® is a registered trademark.

Directions for Use

ANDROFEME® 1% cream contains 10mg testosterone BP per 1mL via measured applicator. A baseline total serum testosterone level, sex hormone-binding globulin (SHBG) and free-testosterone or free-androgen index (FAI) should be measured before initiating treatment.

The following flowchart provides a management algorithm to assist in making a diagnosis prior to initiating therapy.

Does the woman have symptoms consistent with low testosterone levels (e.g., low libido, decreased energy and well-being)?

If YES, initiate evaluation

If NO, evaluate further

Is the woman in an optimum oestrogen state?

If YES, continue evaluation

If NO, initiate oestrogen replacement

Does the woman have laboratory values consistent with a low testosterone level?

If YES, continue evaluation. This should include at least two of three measures of total T, free T, or SHBG and FAI. Androgen values should be in the lowest quartile of normal ranges for reproductive age women (free T <5.0 pmol/L or FAI <2).

If NO, consider alternative treatments or referral

Does the woman have a specific treatable cause for low FAI or Free T (e.g., oral oestrogens, oral contraceptive use)?

If YES, treat the specific cause (e.g., change medications)

If NO, consider androgen replacement therapy


of treatment be undertaken at the conclusion of the third month. Testing at this time should include monitoring of the liver function, haemoglobin and lipids. It is at the physician’s discretion if treatment is to continue.

Lower Torso

Outer Thigh

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