Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Andropatch 2.5 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Andropatch 2.5 mg System contains 12.2 mg testosterone.
Each Andropatch 2.5 mg System delivers *in-vivo* approximately 2.5 mg of testosterone over 24 hours across skin of average permeability. Active surface area is 7.5 cm^2.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Transdermal patch.
Circular, self-adhesive patch with “TDPS-2” and the company logo printed on opposite sides of a central drug reservoir.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Andropatch is indicated for testosterone replacement therapy in use for conditions associated with a deficiency or absence of endogenous testosterone, as seen in primary and secondary hypogonadism.

4.2 Posology and method of administration

Adults and elderly: The usual dose is two 2.5mg Andropatch Systems applied nightly (approximately 10pm) and worn for 24hours, providing approximately 5mg testosterone per day. The dose can be adjusted up to 7.5mg nightly or down to one 2.5mg system nightly depending on the serum testosterone measured in the morning after application. Measurement of serum testosterone should be repeated taking care to ensure proper system adhesion and correct time of application before the dose is adjusted. Three systems per day may be required for men with a higher body weight (>130kg). Treatment in non-virilised patients may be initiated with one system applied nightly. The dose should be adjusted as appropriate.

The duration of treatment and frequency of testosterone measurements is determined by the physician.

The adhesive side of the Andropatch System 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 that may be subjected to prolonged pressure during sleeping or sitting should be avoided. Application to these sites has been associated with burn-like blister reactions (see section 4.8, Undesirable effects).

Do not apply to broken or damaged skin.

Do not apply to the scrotum. The sites of application should be rotated, with an interval of seven days between applications to the same site. The area selected should not be oily, damaged or irritated.

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

Children:
Andropatch is not recommended for use in children, as there is no clinical experience of its use below the age of 15 years.

4.3 Contraindications

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

Know hypersensitivity to testosterone or other constituents of the patch.

Andropatch has not been evaluated in women and must not be used in women.

Testosterone may be harmful to the foetus.

4.4 Special warnings and precautions for use

Initiation of testosterone treatment and its overall direction should only be carried out by specialists.

Testosterone therapy should only be used in male hypogondotrophism in which testosterone levels have been demonstrated to be low.

Elderly men treated with androgens may be at an increased risk for the development of prostatic hyperplasia and prostatic carcinoma.

Elderly men, and others with an increased risk of developing prostate cancer, should be assessed before starting testosterone replacement therapy because testosterone may promote the growth of subclinical prostate cancer.

As in men without testosterone deficiency, patients on testosterone replacement therapy should be periodically evaluated for prostate cancer.

If the patient develops an application site reaction, treatment should be reviewed and discontinued if necessary.

Androgens may reduce thyroxine-binding globulin and PB1 levels without inducing clinical hypothyroidism.

The treatment regimen should avoid undue stimulation of either the physical or mental capacity of the patient. Evidence of excessive sexual stimulation requires discontinuation of therapy.

Care should be taken in patients with skeletal metastases due to the risk of hypercalcaemia/hypercalcuria developing from androgen therapy.

Testosterone may cause a rise in blood pressure and Andropatch should be used in caution in patients with hypertension.

Oedema, with or without congestive heart failure, may result from Androgen treatment in patients with pre-existing cardiac, renal, or hepatic disease. In addition to discontinuation of therapy, diuretic treatment may be required.

Andropatch should be used with caution in patients with ischaemic heart disease, epilepsy and migraine as these conditions may be aggravated.

4.5 Interaction with other medicinal products and other forms of interaction

Barbiturates taken concurrently may stimulate testosterone metabolism, affecting dosage requirements.

When given simultaneously with anticoagulants the anticoagulant effect can increase.

Patients receiving oral anticoagulants require close monitoring especially when androgens are started or stopped.

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

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

4.6 Pregnancy and lactation

Andropatch therapy has not been evaluated in and must not be used in women under any circumstances. Testosterone may be harmful to the foetus. (see section 4.3, Contraindications).

4.7 Effects on ability to drive and use machines

There is no evidence that Andropatch will affect the ability of a patient to drive or to use machines.

4.8 Undesirable effects

In the majority of cases, transient mild to moderate skin reactions have been observed at the site of application at some time during treatment. These include pruritus, irritation with erytherma, induration or burning, rash and allergic contact dermatitis. Burn-like lesions characterised by blisters, skin necrosis, and ulceration that healed over several weeks with scarring in some cases have also been observed.

The burn-like lesions occurred sporadically, usually only at one site, (most commonly over bony prominences or areas that may have been subjected to prolonged pressure during sleeping or sitting). Such lesions should be treated as burns.

As seen with other testosterone treatments, prostate abnormalities, prostate cancer, headache, depression and gastrointestinal bleeding were also observed.

Other known undesirable effects associated with testosterone treatments include hirsuitism, male pattern baldness, seborrhoea, acne, excessive frequency and duration of penile erections, nausea, cholestatic jaundice, increased or decreased libido, anxiety, generalised parasthesia, hypertrichosis, priapism, rash and fluid retention. Oligospermia may occur at high doses.

Prolonged testosterone administration may cause electrolyte disturbances e.g. retention of sodium, chloride, potassium, calcium, inorganic phosphates and water.

4.9 Overdose

This is most unlikely due to the mode of administration. Serum testosterone has a half-life of 70 minutes and therefore falls rapidly once Andropatch Systems are removed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Andropatch delivers physiologic amounts of testosterone producing circulating testosterone concentrations that mimic the normal circadian rhythm of healthy young men.

Testosterone, the primary androgenic hormone is responsible for the normal growth and development of the male sex organs and for the maintenance of secondary sex characteristics. Male hypogonadism results from insufficient secretion of testosterone and is characterised by low serum 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.

Androgens promote retention of nitrogen, sodium, potassium and phosphorus, decreased urinary excretion of calcium, increased protein anabolism, decreased protein catabolism, and are also responsible for the growth spurt of adolescence and for the eventual termination of the linear growth. They stimulate the production of red blood cells by enhancing erythropoietin production.

Exogenous administration of androgens inhibits endogenous testosterone release. With large doses of exogenous androgens, spermatogenesis may be suppressed.

5.2 Pharmacokinetic properties

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

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

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

Upon removal of the Andropatch Systems, serum testosterone concentrations decrease with an apparent half-life of approximately 70 minutes. Hypogonadal concentrations are reached within 24hours following system removal.

5.3 Preclinical safety data

None clinically relevant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified water
Glycerol (E422)
Carbomer Copolymer B
2N Sodium hydroxide (E524)
Ethanol 95%
Glycerol Mono-Oleate
Methyl laurate 96%

Composition of System:

Silicone-coated Polyester Liner
Acrylic adhesive/silicone-coated PET Laminate
Peelable LDPE/aluminium/polyester film
Microporous HMWPE (high molecular weight polyethylene) film
Backing film: inner layer: EVA, Surlyn ® and metallised polyethylene and outer layer: polyethylene layer pigmented with alcohol resistant beige ink to form a beige plastic film.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years
Apply to skin immediately upon removal from a protective pouch.

6.4 Special precautions for storage

Do not store above 25 °C. Store in the original package.

6.5 Nature and contents of container

Each Andropatch 2.5mg System is individually packed into a pouch made from a paper/low density polyethylene (LPDE)/Aluminium foil/LPDE laminate. Andropatch 2.5mg System is supplied in cartons of 10, 30 and 60 pouches.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Andropatch may be discarded with household waste in a manner that avoids accidental contact by others.
Damaged systems should not be used.
The drug reservoir may be burst by excessive heat or pressure.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
Stonemasons Way
Rathfarnham
Dublin 16

8 MARKETING AUTHORISATION NUMBER

PA1077/018/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 03 December 1996
Date of last renewal: 03 December 2006

10 DATE OF REVISION OF THE TEXT

June 2007