SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Testavan 20 mg/g Transdermal gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One pump actuation delivers 1.15 g (1.25 mL) of gel equivalent to 23 mg of testosterone.

Excipient with known effect: 1.15 g gel contains 0.23 g of propylene glycol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Transdermal gel.
Homogenous, translucent to slightly opalescent gel.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Testosterone replacement therapy for adult male hypogonadism, when testosterone deficiency has been confirmed by clinical features and biochemical tests.

4.2 Posology and method of administration

Posology

Testavan should be used only if male hypogonadism has been demonstrated and if other etiology, responsible for the symptoms, has been excluded before treatment is started. Testosterone deficiency should be clearly demonstrated by clinical features (regression of secondary sexual characteristics, change in body composition, asthenia, reduced libido, erectile dysfunction etc.) and confirmed by 2 separate blood testosterone measurements before initiating therapy with any testosterone replacement, including Testavan treatment.

Adult men
The recommended starting dose of Testavan is 23 mg testosterone (one pump actuation) applied once daily. To ensure proper dosing, serum testosterone levels should be periodically measured and dose titrated to maintain serum testosterone levels.

The serum testosterone level should be measured 2-4 hours after dosing approximately 14 days and 35 days after starting treatment or after a dose adjustment. If the serum testosterone concentration is below 17.3 nmol/L (500 ng/dL), the daily Testavan dose may be increased by 1 pump actuation. If the serum testosterone concentration exceeds 36.4 nmol/L (1050 ng/dL), the daily Testavan dose may be decreased by 1 pump actuation.

Dose titration should be based on both serum testosterone levels and the existence of clinical signs and symptoms related to testosterone deficiency.

Elderly
Same dose as for adults. However, it should be taken into account that physiologically testosterone levels are lower with increasing age (see section 4.4).

Maximum recommended dose
The maximum recommended dose is 69 mg testosterone per day, which is equivalent to 3 pump actuations.

Renal and hepatic impairment
There are no studies undertaken to demonstrate the efficacy and safety of this medicinal product in patients with renal or hepatic impairment. Therefore, testosterone replacement therapy should be used with caution in these patients (see section 4.4).

Female population
Testavan is not indicated for use in women.

Paediatric population
Testavan is not indicated in children and has not been clinically evaluated in males under 18 years of age.

Method of administration
Transdermal use.

Testavan is a gel, which should be applied to the upper arm and shoulder, using the applicator. Patients should be instructed not to apply Testavan with fingers or hands.

Priming of new pump
To ensure correct dosing, patients should be instructed to prime each new pump before using it for the first time by pressing the pump head all the way down over a tissue paper until gel appears. Discard the initial gel and 2 additional pump actuations and safely throw away the used tissue paper.

Administration
Testavan should be applied once daily at about the same time, preferably in the morning to clean, dry, intact skin of the upper arm and shoulder using the applicator.

To apply the gel after removal of the applicator lid, the pump head should be pressed all the way down once over the applicator head. Patients should be instructed to only make one pump actuation onto the applicator at a time. The applicator should be used to spread the gel evenly across the maximum surface area of one upper arm and shoulder, making sure not to get any gel on the hands. When more than one pump actuation is required to achieve daily dose, the procedure is repeated to the other upper arm and shoulder.

Dose	**Application method**
23 mg (1 pump depression)	**Apply one** pump actuation to an upper arm and shoulder.
46 mg (2 pump depressions)	**Apply one** pump actuation to an upper arm and shoulder. **Repeat** to apply one pump depression to the opposite upper arm and shoulder.
69 mg (3 pump depressions)	**Apply one** pump actuation to an upper arm and shoulder. **Repeat** to apply one pump depression to the opposite upper arm and shoulder. **Repeat again** to apply the third pump depression to the initial upper arm and shoulder.

Cleaning of the applicator

After use, the applicator should be cleaned with a tissue and the protective lid restored on top of the applicator. The used tissue paper should be safely thrown away and the product stored safely out of reach of children.

Following administration
If the gel was touched with the hands during the application procedure, patients should be instructed to wash their hands with water and soap immediately after applying Testavan.
Patients should be advised to let the application site dry completely before getting dressed.
Patients should be advised to wait at least 2 hours before showering, swimming or bathing to prevent reduced testosterone absorption (see section 4.4).
Wear clothing that covers the application side at all times to prevent accidental transfer to others.

4.3 Contraindications

- Hypersensitivity to the active substance, propylene glycol or to any of the excipients listed in section 6.1.
- Known or suspected carcinoma of the breast or the prostate

4.4 Special warnings and precautions for use

Androgens may accelerate the progression of sub-clinical prostate cancer and benign prostatic hyperplasia.

Prior to initiation of testosterone replacement therapy, all patients must undergo a detailed examination in order to exclude a risk of pre-existing prostatic cancer.
Careful and regular monitoring of the prostate gland and breast must be performed in accordance with recommended methods (digital rectal examination and estimation of serum prostate specific antigen (PSA)) in patients receiving testosterone therapy at least annually and twice yearly in elderly patients and at risk patients (those with clinical or familial factors).

Testavan should be used with caution in cancer patients at risk of hypercalcaemia (and associated hypercalciuria), due to bone metastases. Regular monitoring of serum calcium concentrations is recommended in these patients.

Testavan is not a treatment for male sterility or impotence.

Testosterone levels should be monitored at baseline and at regular intervals during treatment. Clinicians should adjust the dosage individually to ensure maintenance of eugonadal testosterone levels. Certain clinical signs: irritability, nervousness, weight gain, prolonged or frequent erections may indicate excessive androgen exposure requiring dosage adjustment.

There is limited experience on the safety and efficacy of the use of Testavan in patients over 65 years of age. Currently, there is no consensus concerning age specific reference values for testosterone. However it should be taken into consideration that the physiologically testosterone serum levels are lower with increasing age.

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

In patients suffering from severe cardiac, hepatic or renal insufficiency, or ischaemic heart disease treatment with testosterone may cause severe complications characterised by oedema with or without congestive cardiac failure. In this case, treatment must be stopped immediately.

Clotting disorders:

Testosterone should be used with caution in patients with thrombophilia, as there have been post-marketing studies and reports of thrombotic events of these patients during testosterone therapy.

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

There are published reports of increased risk of sleep apnoea in hypogonadal men treated with testosterone esters, especially in those with risk factors such as obesity or chronic respiratory disease.

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

In patients receiving long-term androgen therapy, the following laboratory parameters should also be monitored regularly: haemoglobin, and haematocrit, liver function tests and lipid profile.

Athletes treated for testosterone replacement in primary and secondary male hypogonadism should be advised that the product contains an active substance which may produce a positive reaction in anti-doping tests. Androgens are not suitable for enhancing muscular development in healthy individuals or for increasing physical ability.

Testavan should not be used in women due to possible virilising effects.

As washing after Testavan administration reduces testosterone levels, patients are advised not to wash or shower for at least 2 hours after applying Testavan. When washing occurs up to 2 hours after the gel application, the absorption of testosterone may be reduced.

Testavan contains propylene glycol, which may cause skin irritation.

Alcohol based products including Testavan are flammable; therefore avoid fire, flame or smoking until the gel has dried.

Potential for Transfer
If no precaution is taken, testosterone gel can be transferred to other persons by close skin to skin contact, resulting in increased testosterone serum levels and possibly adverse effects (e.g. growth of facial and/or body hair, acne, deepening of the voice, irregularities of the menstrual cycle) in case of repeat contact (inadvertent androgenisation).

The physician should inform the patient carefully about the risk of testosterone transfer and about safety instructions (see below). Testavan should not be prescribed in patients with a major risk of non-compliance with safety instructions (e.g. severe alcoholism, drug abuse, severe psychiatric disorders).

This transfer is avoided by wearing clothes covering the application area or showering prior to contact.

As a result, the following precautions are recommended:
For the patient:

- use the cap applicator for hands-free administration to reduce the risk of secondary exposure to testosterone.
- if the gel was touched with the hands during the application procedure, wash hands thoroughly with soap and water after applying the gel.
- cover the application area with clothing once the gel has dried.
- shower before any situation in which skin to skin contact with another person is foreseen.

For people not being treated with Testavan:

- in the event of contact with an application area which has not been washed or is not covered with clothing, wash the area of skin onto which testosterone may have been transferred as soon as possible, using soap and water.

- report the development of signs of excessive androgen exposure such as acne or hair modification.

To guarantee partner safety, the patient should be advised for example to observe a long interval between Testavan application and sexual intercourse, to wear a T-shirt covering the application site during contact period, or to shower before sexual intercourse.

Furthermore, it is recommended to wear a T-shirt covering the application site during contact periods with children in order to avoid a contamination risk of children's skin.

Pregnant women must avoid any contact with Testavan application sites. In case of pregnancy of the partner, the patient must reinforce his attention to the precautions for use (see section 4.6).

Patients must be cautioned to minimise use of body lotion and sunscreen products at the area of application, at and just after application of Testavan gel.

Laboratory test interactions: Androgens may decrease concentrations of thyroxin-binding globulins, resulting in decreased total thyroxine (T4) serum concentration and increased resin uptake of triiodothyronine (T3) and T4. Free thyroid hormone concentration remains unchanged and there is no clinical evidence of thyroid dysfunction.

4.5 Interaction with other medicinal products and other forms of interaction

When androgens are given simultaneously with anticoagulants, the anticoagulant effects can increase. Patients receiving oral anticoagulants require close monitoring of their international normalized ratio (INR) especially when androgen treatment is started or stopped.

The concurrent administration of testosterone with adrenocorticotropic hormone (ACTH) or corticosteroids may increase likelihood of oedema; thus these drugs should be administered with caution, particularly in patients with cardiac, renal or hepatic disease.

Improved insulin sensitivity may occur in patients treated with androgens who achieve normal testosterone plasma concentrations following replacement therapy.

Interaction studies with body lotion and sunscreen products have not been performed.

4.6 Fertility, pregnancy and lactation

Testavan is intended for use by men only.

No clinical trials have been conducted with Testavan for assessment of male fertility. Spermatogenesis may be reversibly suppressed with Testavan (see section 5.3).

Pregnant women should avoid skin contact with Testavan application sites (see section 4.4).
In the event that unwashed or unclothed skin to which Testavan has been applied does come into direct contact with the skin of a pregnant woman, the general area of contact on the woman should be washed with soap and water immediately.
Testosterone may induce virilising effects on the foetus.

4.7 Effects on ability to drive and use machines

Testavan has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a. *Summary of the safety profile*

The most commonly reported adverse reactions in phase 2 and phase 3 clinical trials lasting up to 9 months were application site reactions (4%) including: rash, erythema, pruritus, dermatitis, dryness, and skin irritation. The majority of these reactions were mild to moderate in severity.

b. Tabulated summary of adverse events

Adverse drug reactions reported in 1 - <10% of patients treated with Testavan in the phase 2 and phase 3 clinical trials are listed in the following table. All adverse reactions reported with a suspected relationship are listed by class and frequency.

MedDRA System Organ Class	**Common (>1/100 to <1/10)**
General disorders and administration site conditions	Application site reaction (including rash, erythema, pruritus, dermatitis, dryness, and skin irritation)
Investigations	Blood triglycerides increased/hypertriglyceridaemia, PSA increased, red blood cell count increased, haematocrit increased, haemoglobin increased
Vascular disorders	Hypertension

According to literature and spontaneous reporting from testosterone gels, other known undesirable effects are listed in the below table:

MedDRA System Organ Class	**Adverse Reactions – Preferred term**
Blood and lymphatic system disorders	Polycythaemia, anaemia
Psychiatric disorders	Insomnia, depression, anxiety, aggression, nervousness, hostility
Nervous system disorders	Headache, dizziness, paraesthesia
Vascular disorders	Hot flushes (vasodilation), deep vein thrombosis
Respiratory, thoracic and mediastinal disorders	Dyspnoea, sleep apnoea
Gastrointestinal disorders	Nausea
Skin and subcutaneous tissue disorders	Various skin reactions may occur including acne, seborrhoea and balding (alopecia), sweating, hypertrichosis
Musculoskeletal and connective tissue disorders	Musculoskeletal pain, muscle cramps
Renal and urinary disorders	Urination impaired, urinary tract obstruction
Reproductive system and breast disorders	Gynaecomastia, erection increased, testis disorder, oligospermia, benign prostatic hyperplasia, libido changes (therapy with high doses of testosterone preparations commonly reversibly interrupts or reduces spermatogenesis, thereby reducing the size of the testicles; testosterone replacement therapy of hypogonadism can in rare cases cause persistent, painful erections (priapism), prostate abnormalities, prostate cancer*)

General disorders and administration site conditions	Asthenia, malaise, application site reaction. High dose or long-term administration of testosterone occasionally increases the occurrences of water retention and oedema; hypersensitivity reactions may occur.
Investigations	Weight increase, elevated PSA, elevated haematocrit or elevated haemoglobin
Metabolism and nutrition disorders	Electrolyte changes (retention of sodium, chloride, potassium, calcium, inorganic phosphate and water) during high dose and/or prolonged treatment.
Hepatobiliary disorders	Jaundice and liver function test abnormalities.

* Data on prostate cancer risk in association with testosterone therapy are inconclusive.

Because of the alcohol contained in the product, frequent applications to the skin may cause irritation and dry skin.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V*

4.9 Overdose

No case of overdose with Testavan has been reported in clinical trials.

Symptoms
Clinical signs such as irritability, nervousness, weight gain, prolonged or frequent erection can indicate overexposure to androgen and serum testosterone levels should therefore be measured.

Treatment
Treatment of overdosage consists of discontinuation of Testavan together with appropriate symptomatic and supportive care.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Androgens, ATC code: G03B A03

Testosterone and dihydrotestosterone (DHT), endogenous androgens, are responsible for the normal growth and development of the male sex organs and for the maintenance of secondary sex characteristics. These effects include the growth and maturation of the prostate, seminal vesicles, penis and scrotum; the development of male hair distribution on the face, chest, axillae and pubis; laryngeal enlargement, vocal chord thickening, alterations in body musculature and fat distribution.

Insufficient secretion of testosterone due to testicular failure, pituitary pathology or gonadotropin or luteinising hormone-releasing hormone deficiency results in male hypogonadism and low serum testosterone concentration. Symptoms associated with low testosterone include decreased sexual desire with or without impotence, fatigue, loss of muscle mass, mood depression and regression of secondary sexual characteristics.

Restoring testosterone levels to within the normal range can result in improvements over time in muscle mass, mood, sexual desire, libido and sexual function including sexual performance and number of spontaneous erections.

During exogenous administration of testosterone to normal males, endogenous testosterone release may be decreased through feedback inhibition of pituitary luteinising hormone (LH). With large doses of exogenous androgens, spermatogenesis may also be suppressed through inhibition of pituitary follicle stimulating hormone (FSH).

Androgen administration causes retention of sodium, nitrogen, potassium, phosphorus and decreased urinary excretion of calcium. Androgens have been reported to increase protein anabolism and decrease protein catabolism. The nitrogen balance is improved only with sufficient intake of calories and protein. Androgens have been reported to stimulate production of red blood cells by enhancing the production of erythropoietin.

5.2 Pharmacokinetic properties

Testavan delivers physiologic amounts of testosterone, which provide a level of circulating testosterone similar to the normal level in healthy men (i.e., 300-1050 ng/dL). Testavan was evaluated in a multi-center, open-label, 120 day Phase 3 clinical study (study 000127) in 159 hypogonadal men ages 18 to 75 years (mean age 54.1 years). Subjects were white (77%), black (20%), Asian (2%), and multiracial (1%). In the phase 3 study, at the end of a 90 day treatment period during which the dose of Testavan could be titrated based on total testosterone concentrations, 76.1% of men had average testosterone concentrations over a 24 hour period (Cave) within the eugonadal range (300 – 1050 ng/dL).

The mean testosterone concentration profile on Day 90 is shown in Figure 1, while the pharmacokinetic parameters for total testosterone on Day 90 are summarised for each Testavan dose in Table 11.

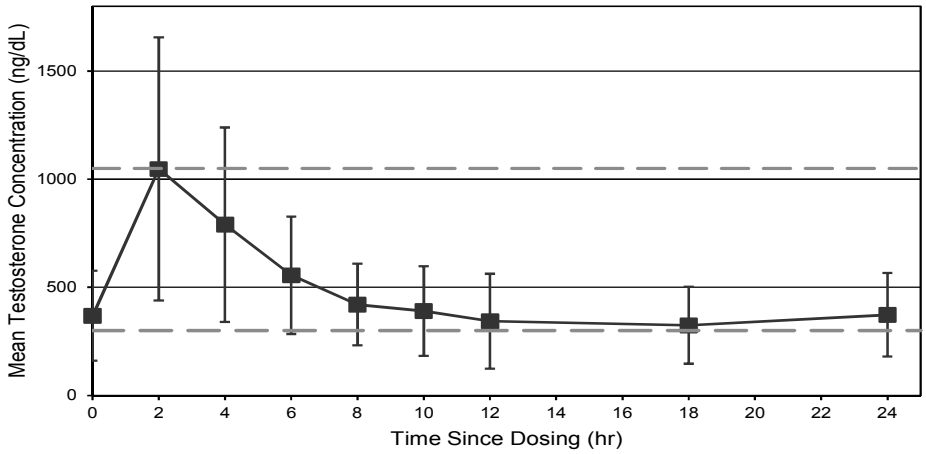


Figure 1 Mean ±SD serum concentrations of testosterone on day 90 after dose titration of Testavan

Table 1 Pharmacokinetic parameters for total testosterone on day 90 after titration, study 000127 full analysis set

Testavan Dose on Day 90	N	C_{min} (ng/dL) Mean ±SD	C_{ave} (ng/dL) Mean ±SD	C_{max} (ng/dL) **Mean ±SD**	T_{max} (hr) **Median**
23 mg	5	191 ± 49	368 ± 121	721 ± 254	4.02
46 mg	45	277 ± 140	506 ± 207	1,228 ± 640	2.02
69 mg	89	229 ± 82	438 ± 164	1,099 ± 595	2.08

C_{min}: minimum concentration; C_{ave}: average concentration over a 24 hour period; C_{max}: maximum concentration; T_{max}: time of maximum concentration; SD: standard deviation

Absorption
Testavan provides transdermal delivery of testosterone, with a median Tmax of approximately 2-4 hours after dosing. Total testosterone concentrations return to pre-dose values approximately 12 hours after application and no accumulation occurs after daily application for 10 days.

Phase 2 study results show that total testosterone concentrations increased with increasing dose after daily application of 23, 46 and 69 mg Testavan.

Distribution
Circulating testosterone is chiefly bound in the serum to sex hormone-binding globulin (SHBG) and albumin. The albumin-bound fraction of testosterone easily dissociates from albumin and is presumed to be biologically active. The portion of testosterone bound to SHBG is not considered biologically active. Approximately 40% of testosterone in plasma is bound to SHBG, 2% remains unbound (free) and the rest is bound to albumin and other proteins.

Biotransformation
There is considerable variation in the half-life of testosterone, as reported in the literature, ranging from ten to 100 minutes.
Testosterone is metabolised to various 17-keto steroids through two different pathways. The major active metabolites of testosterone are oestradiol and dihydrotestosterone (DHT).

Elimination
About 90% of testosterone given intramuscularly is excreted in the urine as glucuronic and sulphuric acid conjugates of testosterone and its metabolites; about 6% of a dose is excreted in the faeces, mostly in the unconjugated form.

Effect of Showering
Showering 1 hour and 2 hours following Testavan administration decreased Cave by 19.2% and 14.3%, respectively, compared with subjects who did not shower after Testavan administration. Showering 6 hours following Testavan administration did not result in a decrease in Cave.

5.3 Preclinical safety data

Toxicological studies have not revealed other effects than those which can be explained on the base of the hormone profile of TESTAVAN.

Fertility studies in rodents and primates have shown that treatment with testosterone can impair male fertility by suppressing spermatogenesis in a dose dependent manner.

Testosterone has been found to be non-mutagenic in vitro using the reverse mutation model (Ames test) or Chinese hamster ovary cell line. A relationship between androgen treatment and certain cancer forms has been found in laboratory animals. Data in rats have shown increased incidences of prostate cancer after treatment with testosterone.

Sex hormones are known to facilitate the development of certain types of tumour induced by known carcinogenic agents. No correlation between these findings and the actual risk in human beings has been established.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol (96%)
Water, purified
Propylene glycol (E 1520)
Diethylene glycol monoethyl ether
Carbomer 980
Trolamine
Disodium edetate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Testavan is supplied in a multidose container consisting of a metering pump with a laminate foil pouch in a bottle, and is provided with a cap applicator with a hygienic lid. The pump is composed of polypropylene, ethylene propylene diene monomer and stainless steel and the pouch is a polyethylene/polyethylene terephthalate/aluminium/polyethylene laminate encased in a rigid polypropylene bottle.

The product is available in packs of one multidose container containing 56 doses

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]

LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

METERED DOSE DISPENSER

1. NAME OF THE MEDICINAL PRODUCT

Testavan®
20 mg/g transdermal gel
testosterone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pump actuation delivers 1.15 g (1.25 ml) gel equivalent to 23 mg of testosterone

3. LIST OF EXCIPIENTS

Other ingredients: ethanol 96%, purified water, propylene glycol (E1520), diethylene glycol monoethyl ether, carbomer 980, trolamine, disodium edetate

4. PHARMACEUTICAL FORM AND CONTENTS

Contains 85.5 g transdermal gel.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Prime the pump before first use.

Read the package leaflet before use.

For transdermal use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Content is flammable.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

N/A

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

N/A

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

N/A

16. INFORMATION IN BRAILLE

N/A

17. UNIQUE IDENTIFIER – 2D BARCODE

N/A

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

N/A

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Testavan®
20 mg/g transdermal gel
testosterone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pump actuation delivers 1.15 g (1.25 ml) gel equivalent to 23 mg of testosterone

3. LIST OF EXCIPIENTS

Other ingredients: ethanol, purified water, propylene glycol, diethylene glycol monoethyl ether, carbomer homopolymer type C, trolamine, disodium edetate

4. PHARMACEUTICAL FORM AND CONTENTS

Contains 85.5 g transdermal gel.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Prime the pump before first use.

Read the package leaflet before use.

For transdermal use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Content is flammable.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

N/A

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

N/A

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

N/A

16. INFORMATION IN BRAILLE

Testavan

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

< PC: {number} [product code]
SN: {number} [serial number]
NN: {number} [national reimbursement number or other national number identifying the medicinal product]>

PACKAGE LEAFLET

Package leaflet: Information for the user

Testavan® 20 mg/g transdermal gel
testosterone

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Testavan is and what it is used for

What Testavan is
Testavan is a clear gel that contains testosterone, a male hormone produced naturally in your body.

Testavan is used to replace testosterone in adult men when you do not produce enough natural testosterone – this is called "hypo-gonadism". The medicine helps to raise your testosterone to normal levels.

What testosterone does
Testosterone is made naturally in your body in your testicles.
- It helps produce sperm and to develop and maintain male features such as a deep voice and body hair.
- It is necessary for normal sexual function and sex drive.
- It also helps to maintain muscle size and strength.

What Testavan is used for
Testavan is used in men for testosterone replacement to treat various health problems caused by a lack of testosterone (male hypogonadism). This should be confirmed by two separate blood testosterone measurements and also include clinical signs and symptoms such as:
- impotence
- infertility
- low sex drive
- tiredness
- depressive moods
- bone loss caused by low hormone level
- partial loss of secondary sex characteristics, such as changes in your voice, changes in the fat distribution
- and partial loss of face and body hair

2. What you need to know before you use Testavan

Who can use Testavan
- Only men can use Testavan.
- Young men under the age of 18 years should not use this medicine.
- This medicine should not be used by females of any age.
- Do not allow women (especially women that are pregnant or breast-feeding) or children to come into contact with Testavan gel or the areas of skin where Testavan has been applied.

Do not use Testavan:
- if you are allergic to testosterone or any of the other ingredients of this medicine (listed in section 6)
- if you have or are suspected of having prostate cancer
- if you have or are suspected of having breast cancer (a rare condition for men).

Warnings and precautions
Testosterone treatment can speed up the progress of pre-existing prostate cancer. Your doctor will do the necessary tests before you can use Testavan and do follow-up check by carrying out periodic blood tests and prostate examinations.

Talk to your doctor or pharmacist before using Testavan, if any of the following applies to you:
- you have difficulty in passing water (urinating) due to an enlarged prostate gland
- you have bone cancer - your doctor will check your calcium levels
- you have high blood pressure, or if you are treated for high blood pressure, as Testavan may cause a rise in blood pressure
- you have severe heart, liver or kidney disease, as treatment with Testavan may cause severe complications in the form of water retention in your body sometimes accompanied by (congestive) heart failure (fluid overload in the heart)
- you have ischaemic heart disease (which affects the supply of blood to the heart)
- you have a blood clotting problems called “thrombophilia” (a problem of blood coagulation – this increases the risk of getting blood clots in your blood vessels (“thrombosis”)
- you have epilepsy
- you have migraines
- you have breathing difficulties when you sleep - these are more likely to happen if you are overweight or have long term lung problems

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before using Testavan – using this medicine may make these conditions worse.

If you develop reactions on your skin where you applied the Testavan, go back to your doctor to seek advice. It may be necessary to stop the treatment with Testavan.

Do not use Testavan to treat male sterility or impotence in men with normal testosterone levels in their blood.

The following blood checks should be carried out by your doctor before and/or during the treatment: testosterone blood levels, full blood count.

If you are an athlete, be aware that this product may produce a positive reaction in anti-doping tests. Testosterone must not be used to increase muscles or improve physical strength in healthy individuals.

At the time of, and just after, the daily application of Testavan, do not apply moisturisers or sunscreen products to the area where you have put the gel

How to prevent transfer of Testavan to someone else

Testavan can transfer to others by close skin-to-skin contact. This may result in increased testosterone levels in their body – this can be dangerous. This can happen from one contact – but it can also build up bit by bit with small amounts of contact over time.

- This is especially important for women and children – they normally only have low levels of testosterone in their bodies
- Pregnant women must not come into contact with Testavan. If your partner is pregnant you must be careful and protect her from any contact with the medicine and the application area.

To stop the gel being transferred from your skin to someone else, recommended you should:

- use the applicator to apply the medicine rather than your fingers
- wash your hands with water and soap straight away if you do get any Testavan on your hands
- cover where you have put the gel with clothing - once the gel has dried
- have a bath or shower, or wear clothing to cover the gel application site (such as a T-shirt), before having close skin-to-skin contact with anyone
- leave a long period of time between using the gel and having sex or other close skin to skin contact with anyone.

What to do if someone else is exposed to Testavan

If someone touches the gel or has skin-to-skin contact where you have put the gel, they should wash their area of skin with soap and water as soon as possible. The longer that the gel is in contact with the skin before washing, the greater the chance that the person will absorb some testosterone.

If Testavan has been transferred to someone else, then look out for any changes in the body or behaviour of people close to you. If anyone close to you gets any of the following signs, they should see their doctor:

- acne
- deepening of the voice
- growth of facial or body hair
- changes in their monthly period
- early puberty, genital enlargement or changes in level of sexual behaviour of children

Other medicines and Testavan

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. This includes medicines obtained without a prescription and herbal medicines. Testavan may affect how these medicines work and you may need to have your doses adjusted.

In particluar, tell your doctor or pharmacist if you are taking:

- Medicines to thin your blood (anti-coagulants) - Testavan may increase the effects of these drugs
- corticosteroids or any other medicines that may increase the production of these hormones. Both corticosteroids and Testavan may cause your body to hold on more water
- insulin to control your blood sugar levels (in diabetes); you may need to reduce your dose of insulin when you are in treatment with Testavan.

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before using Testavan

Pregnancy, breast-feeding and fertility

Testavan is not intended for use by pregnant or breastfeeding women.

If your partner is or becomes pregnant, you **must** follow the advice above under the heading **'How to prevent transfer of TESTAVAN to someone else'**.

Pregnant women must avoid **any** skin contact with Testavan application sites in men. This medicine may cause damage to the unborn baby.

Breast-feeding women must avoid **any** contact with Testavanapplication sites in men.

Sperm production may be reversibly suppressed with Testavan.

Testavan contains propylene glycol
This medicine contains propylene glycol, which may cause skin irritation.

3. How to use Testavan

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to use

- The recommended starting dose of Testavan is 23 mg testosterone (one pump press) applied once daily at approximately the same time each day preferably in the morning - but some patients may require a higher dose.
- The maximum recommended dose is 69 mg testosterone daily (three pump presses).

The correct dose of Testavan that you need will be decided by your doctor – they will do this by measuring two things regularly:
- the levels of testosterone in your blood
- How well the medicine is working for you.

Talk to your doctor if you feel that the effects of the medicine is too strong or too weak.

Using this medicine
It is important that you read and follow these directions on how to use Testavan properly.

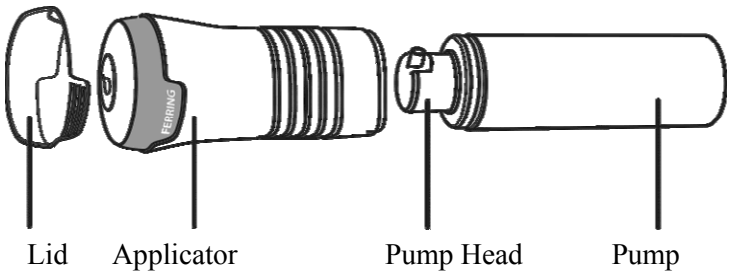
Apply Testavan on your skin using the applicator. This is called "trans-dermal use" – the medicine goes through your skin into your body.

Apply the medicine only to clean, dry, normal healthy skin on your shoulders or upper arms.

Never apply Testavan to:
- your penis and testicles
- to skin that is broken or damaged
-open sores, wounds or irritations.

<u>Supplies you will need</u>

- Testavan gel pump kit. **See Picture A**.
- Box of tissues.

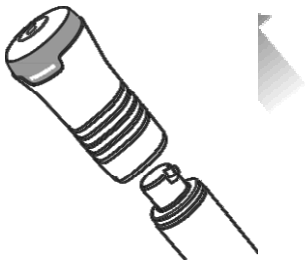


Picture A

Priming your gel pump – first time only

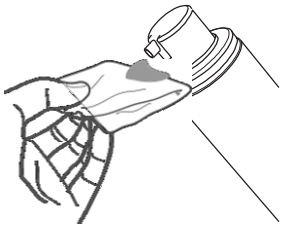
Before using a **new** Testavan pump, you need to get it ready to use. This is called "priming" the pump:

- Take off the applicator from the pump. **See Picure B**.



Picture B

- Prime the pump by pressing the pump head all the way down over a tissue. Repeat until gel appears. **See Picture C**.



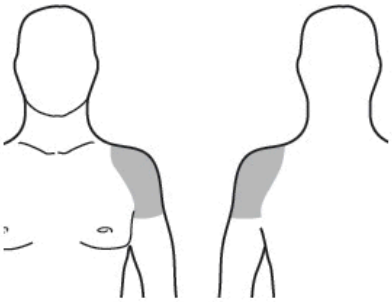
Picture C

- Do 2 additional pump presses. This will help make sure your dose is correct.
- **Do not use any gel from priming because it might not be the right dose.**
- Safely throw away the used tissues in your household rubbish to prevent transferring to others including children or pets.
- Your Testavan pump is now ready to use.

For daily dosing follow steps 1-4

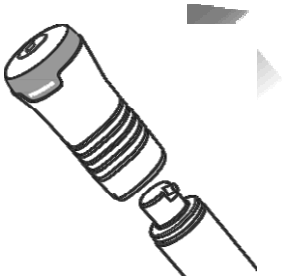
Step 1: Preparing to apply your Testavan gel

- Select a clean, dry, normal healthy area of the skin on the upper arm and shoulder that would be covered by a short sleeve t-shirt. **See Picture D**.
- Use Testavan gel **only** on the upper arm and shoulder.



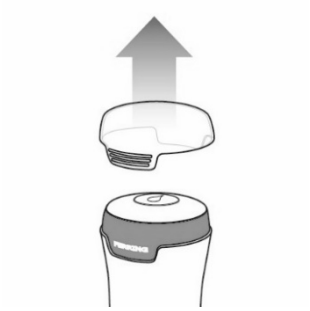
Picture D

- Take off the applicator from the pump **See Picture E**.



Picture E

- Take off the lid from the applicator **See Picture F**.



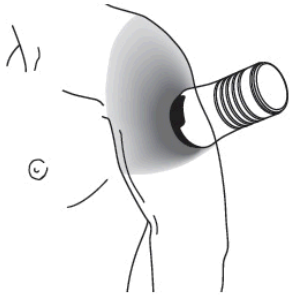
Picture F

Step 2: Applying your Testavan gel

- Hold the pump with the nozzle facing the applicator surface.
- Press the pump head all the way down **once**. **See Picture G**.

Picture G

- Use the applicator to spread the gel evenly across one upper arm and shoulder, making sure not to get any gel on your hands. **See Picture H**.
- Clean up any spills with a tissue. Safely throw away used tissues in your household rubbish to prevent transfer to others including children or pets.



Picture H

Find your dose as prescribed by your doctor in the table below.

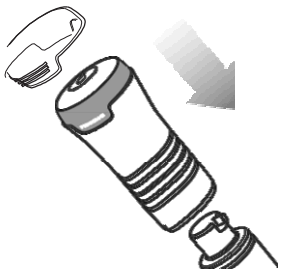
Dose	**How to apply**
23 mg (1 pump press)	Apply one pump press as shown in **Step 2 – do this once**.
46 mg (2 pump presses)	**Apply one pump press as shown in Step 2.** **Repeat** to apply another pump press – put on the opposite upper arm and shoulder.
69 mg (3 pump presses)	**Apply one pump press as shown in Step 2.** **Repeat** to apply one pump press – put on the opposite upper arm and shoulder. **Repeat** again to apply the third pump press to the first upper arm and shoulder that you used.

Step 3: Cleaning your Testavan applicator

- After use, clean the applicator with a tissue. **See Picture I.**

Picture I

- Safely throw away used tissue in your household rubbish. Be careful to prevent transfer to others including children or pets.
- **REMEMBER** to put the lid back on the applicator and put the applicator back on the pump. **See Picture J**.



Picture J

- Store the product safely and out of reach of children.

Step 4: After applying your Testavan

- **Wash your hands with soap and water straight away, if you got gel on them.**
- Testavan gel is flammable until dry. Let the Testavan gel dry before smoking or going near an open flame.
- Let the application site dry completely before getting dressed.
- Wear clothing that covers the application site at all times to prevent accidental transfer to others.
- **Wait at least 2 hours** before showering, swimming or bathing.
- Wash the application site with soap and water before any situation where skin-to-skin contact of the application site with another person is likely.

If you use more Testavan than you should
If you have applied too much medicine by mistake, wash the application area with soap and water as soon as you realise.
Only use the amount of medicine prescribed by your doctor. If you feel irritable, nevous, gain weight, get long lasting or frequent erections – these may be signs that you are using too much.

If you forget to use Testavan
Do not use a double dose to make up for a forgotten dose.
- If your next dose is less than 12 hours away, do not take the missed dose. Then takeyour next dose as normal.
- If it is more than 12 hours until your next dose, take the dose that you have missed. Continue as normal the following day.

If you stop using Testavan
Talk to your doctor before you stop taking this medicine.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Common (may affect up to 1 in10 people)
- skin irritation where the gel has been applied (including rash, dryness and redness)
- high levels of triglycerides in the blood
- increased blood pressure
- increased Prostatic Specific Antigen (PSA). PSA is a protein produced by the prostate, which can be used to detect prostate disease
- increase in red blood cell count, increased haematocrit (percentage of red blood cells in blood) and haemoglobin the component of red blood cells that carries oxygen)

Other known undesirable effects associated with testosterone treatment include:
acne, seborrhoea, baldness, sweating, increased body hair growth, skin tickling or numbness, headache, dizziness, nausea, hot flushes, fluid retention (such as swelling of ankles), weight gain, sleep apnoea, shortness of breath, hypersensitivity reactions, feeling sick/unwell, changes to your mood (such as aggression, hostility, nervousness, anxiety, depression), sleeplessness, muscular pain or cramp, development of breasts, decrease in red blood cells, blood clots, jaundice (liver problems which sometimes may be associated with yellowing of the skin and the whites of the eyes), abnormal liver function tests.
Sex drive changes, erection increased, priapism (prolonged and painful erections), testis disorder, reduced number of sperm, difficulty passing urine, changes to your prostate gland, prostate cancer (there is no convincing evidence that testosterone replacement in hypogonadal men induces prostate cancer; however, testosterone therapy is to be avoided in men already known or thought to have prostate cancer).
Prolonged testosterone administration may cause changes in the levels of salts (electrolytes) and water in the body.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Testavan

Keep this medicine out of the sight and reach of children.

This medicine does not require any special temperature storage conditions.

Do not use this medicine after the expiry date which is stated on the multidose container label and the outer carton after Exp. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Testavan contains
The active substance is testosterone.
The other excipients are: ethanol 96%, propylene glycol (E1520), diethylene glycol monoethyl ether, carbomer 980, trolamine, disodium edetate, purified water.

Each pump press delivers 1.15 g gel (1.25 ml) containing 23 mg of testosterone.

What Testavan looks like and contents of the pack
Testavan is a homogenous, translucent to slightly opalescent gel.

The pump is available in packs of one multidose container consisting of a metering pump and a cap applicator with a hygiene lid.
Each pump contains 85.5 g Testavan gel and is capable of dispensing 56 metered doses.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
[To be completed nationally]

Manufactured by:
Ferring Controlled Therapeutics Limited
1 Redwood Place, Peel Park Campus
East Kilbridge, G74 5PB
United Kingdom

 **CAP applicator:**
Ferring Pharmaceuticals A/S
Kay Fiskers Plads 11
2300 Copenhagen S
Denmark

CE

This medicinal product is authorised in the Member states of the EEA under the following names:

{Name of the Member State} {name of the medicinal product}
{Name of the Member State} {name of the medicinal product}

This leaflet was last revised in:

[To be completed nationally]