Supporting Document for Testogel® (testosterone) 16.2mg/g, gel in pump

Details of Drug[1]

Name of the medicinal product	TESTOGEL 16.2 mg/g gel
Qualitative and quantitative composition	One gram of gel contains 16.2 mg testosterone. One pump actuation delivers 1.25 g of gel containing 20.25 mg of testosterone.
Brand name	Testogel 16.2mg/g
Manufacturer	Besins Healthcare (UK) Ltd Lion Court 25 Proctor Street London WC1V 6NY
Is the drug licensed in the UK?	Yes

Indications[1]

Licensed Indication	Testosterone replacement therapy for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests [1]

Mechanism of action[1]

Mechanism of action	Testogel 16.2mg/g is a hydroalcoholic gel. Gels such as this when applied to the skin are rapidly absorbed into the stratum corneum layer which forms a reservoir that then acts as a rate-controlling membrane. Gel is then gradually diffused from this skin reservoir over several hours. Steady state blood testosterone levels are reached usually by the second day of treatment with Testogel 16.2 mg/g [1,2]

1. Testogel 16.2mg/g Summary of Product Characteristics, Besins Healthcare, July 2018 https://www.medicines.org.uk/emc/product/8919/smpc Accessed July 2019
2. Wang C et al. J Clin Endocrinol Metab 2000;85:964-969

Dosage regimen and monitoring requirements of Testogel® (testosterone) 16.2mg/g[1]

Dosage Regimen	Transdermal use. Adult and elderly men The recommended dose is two pump actuations of gel (i.e. 40.5 mg of testosterone) applied once daily at about the same time, preferably in the morning. The daily dose should be adjusted by the doctor depending on the clinical or laboratory response in individual patients, not exceeding four pump actuations or 81 mg testosterone per day. The adjustment of posology should be achieved by increments of one pump actuation of gel. The dose should be titrated based on the pre-dose morning testosterone blood levels. Steady state blood testosterone levels are reached usually by the second day of treatment with TESTOGEL 16.2 mg/g. In order to evaluate the need to adjust the testosterone dosage, blood testosterone levels should be measured in the morning before application of the product, after the steady state is reached. Testosterone blood levels should be assessed periodically. The dose may be reduced if the testosterone blood levels are raised above the desired level. If the levels are low, the dosage may be increased stepwise, to a daily administration of 81 mg of testosterone (four actuations of gel) per day. The application should be administered by the patient himself, onto clean, dry, healthy skin over right and left upper arms and shoulders. The gel should be simply spread on the skin gently as a thin layer. It is not necessary to rub it on the skin. Allow to dry for at least 3-5 minutes before dressing. Do not apply to the genital areas as the high alcohol content may cause local irritation. To obtain a full first dose, it is necessary to prime the canister pump. To do so, with the canister in the upright position, slowly and fully depress the actuator three times. Safely discard the gel from the first three actuations. It is only necessary to prime the pump before the first dose. After the priming procedure, fully depress the actuator once for delivering 1.25 g of Testogel 16.2 mg/g into the palm of the hand and then apply to the upper arms and shoulders.
Monitoring requirements	Prior to initiation of therapy, all patients must undergo a detailed examination in order to exclude a risk of pre-existing prostate cancer. During treatment, careful and regular monitoring of prostate gland and breast must be performed (digital rectal examination [DRE]and estimation of serum prostate specific antigen [PSA]) at least once yearly and twice yearly in elderly and at-risk patients (those with clinical or familial risk factors) Testosterone level should be monitored at baseline and at regular intervals during treatment. Clinicians should adjust the dosage individually to ensure maintenance of eugonadal testosterone levels. Therapy should be discontinued if the blood testosterone levels consistently exceeds the normal range at the lowest daily dose of 20.25 mg (1.25 g gel, equivalent to one pump actuation) or if blood testosterone levels in the normal range cannot be achieved with the highest dose of 81 mg (5 g gel, equivalent to four pump actuations). Beside laboratory tests of the testosterone concentrations in patients receiving long-term androgen therapy the following laboratory parameters should also be monitored regularly: haemoglobin, haematocrit (to detect polycythaemia), liver function tests, and lipid profile.

1. Testogel 16.2mg/g Summary of Product Characteristics, Besins Healthcare, July 2018 https://www.medicines.org.uk/emc/product/8919/smpc Accessed July 2019

Guidelines associated with testosterone therapy – Screening & Diagnosis [5-11]

In recent years, established specialist medical societies have produced guidance on the use of testosterone therapy (TTh) in men with testosterone deficiency (TD). These include:

- The British Society for Sexual Medicine (BSSM)[5]
- The European Association of Urology (EAU)[6]
- American Urological Association (AUA)[7]
- The Endocrine Society (ES)[8]

There is overall consensus among the guidance produced by these expert groups that a diagnosis of Testosterone Deficiency (TD) should only be made when patients have low total testosterone (TT) levels (using 2 Total Testosterone (TT) measurements taken on separate occasions, taken in early morning), combined with symptoms and/or signs [5-8]

The majority of guidelines also recommend routine screening for Testosterone Deficiency (TD) in men with the following conditions:

- Erectile Dysfunction (ED)
- Type 2 diabetes mellitus (T2DM)
- Obesity
- Chronic opiate use [5,7-10]

The British Society for Sexual Medicine guidelines on adult testosterone deficiency recommend basing decisions on therapy according to published action levels rather than laboratory reference ranges. The rationale for this is because reference ranges quoted by laboratories represent the normal population and that the action levels recommended by the BSSM refer to men with clinical symptoms of Testosterone Deficiency (TD).[5]

The action levels quoted by the BSSM are as follows:[5]

- Total Testosterone level <8 nmol/L or Free Testosterone level <0.180 nmol/L
    - **Usually requires Testosterone Therapy**
- Total Testosterone level >12 nmol/L or free testosterone level >0.225 nmol/L
    - **Does not require Testosterone Therapy**
- Total Testosterone level between 8-12 nmol/L or free testosterone level 0.180-0.225 nmol/L
    - **May require a trial of Testosterone Therapy for a minimum of 6 months**

BSSM guidelines also state:[5]

- A free testosterone (FT) level lower than 0.225 nmol/L provides supportive evidence for Testosterone therapy in the presence of appropriate symptoms.

In addition, the 2018 British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction state that low testosterone is a frequent reason for failure to respond to Phosphodiesterase 5 inhibitors (PDE5i) and that correction of low testosterone levels <10.4nmol/L has been shown in multiple studies to restore the response to PDE5Is.[11]

Guidelines associated with testosterone therapy (TTh) – Benefits & Risks of Testosterone Therapy (TTh) in Testosterone Deficiency (TD) Patients [5]

British Society for Sexual Medicine (BSSM) Guidelines state:

- Beyond 6 months there is evidence of benefit for Testosterone Therapy (TTh) in body composition, bone mineralisation, and features of metabolic syndrome.
- Testsosterone Therapy (TTh) improves sexual desire, erectile function & sexual satisfaction.
- Decreases in bone mineral density (BMI) and waist size and improved glycaemic control and lipid profile are observed.
- Trials of Testosterone Therapy should be ≥6 months and maximal benefit is often seen beyond 12 months
- Fully inform the patient about expected benefits and side effects of therapy and facilitate a joint discussion by an informed patient and physician.
- Fully discuss the adverse effect of Testosterone Therapy (TTh) and its effect on future fertility for each patient and his partner and offer alternative treatment as necessary.
- In patients with adult-onset TD, when Testosterone Therapy (TTh) is prescribed, offer weight-loss and lifestyle advice as standard management.
- In severely symptomatic patients with Total Testosterone (TT) levels <8 nmol/L, lifestyle and dietary advice alone is unlikely to produce meaningful clinical improvement within a relevant clinical period.

Guidelines associated with testosterone therapy (TTh) – Follow up & monitoring [5,6,8]

British Society for Sexual Medicine (BSSM) Guidelines state:

- Aim for a target total testosterone (TT) level of 15-30 nmol/L to achieve optimal response.
- Prostate health should be assessed by digital rectal examination (DRE) and prostate specific antigen (PSA) before initiating therapy. Follow-up by PSA testing at 3, 6 and 12 months and DRE 3–12 months after initiating Testosterone Therapy (TTh), and thereafter annually for both.
- Check haematocrit at baseline, 3–6 months after starting treatment, and then annually. If haematocrit is >54% and remains high, consider stopping therapy and reintroducing at a lower dose or switching preparations.
- Assess cardiovascular (CV) risk before Testosterone Therapy (TTh) is initiated and monitor CV risk factors throughout therapy.
- Assess response to therapy at regular intervals within the first year and then annually thereafter.

Guidelines associated with the choice of testosterone therapy (TTh) in the initial treatment of patients with Testosterone Deficiency[12]

International Society for the Study of the Ageing Male (ISSAM) recommendations state:

- The selection of the testosterone therapy should be a joint decision of an informed patient and physician [12]
- Because the possible development of an adverse event (especially elevated haematocrit, or prostate cancer) during treatment requires rapid discontinuation of testosterone therapy, short-acting preparations may be preferred over the long-acting depot preparations in the initial treatment of patients with hypogonadism. [12]

5. Hackett G, et al. J Sex Med 2017;14:1504-23. 6. Dohle GR, et al. Guidelines of Male Hypogonadism. European Association of Urology 2015. Available at: uroweb.org/wp-content/uploads/18-Male-Hypogonadism_LR1.pdf Accessed May 2019. 7. Mulhall JP, et al. American Urological Association 2018. 8. Bhasin S, et al. J Clin Endocrinol Metab 2018;103(5):1715-44. 9. Garvey TW, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for Comprehensive Medical Care of Patients with Obesity. Available at: aace.com/files/guidelines/ObesityExecutiveSummary.pdf Accessed May 2019 10. American Diabetes Association. Diabetes Care 2019;42(Suppl.1):S34–S45. Available at: care.diabetesjournals.org/content/diacare/suppl/2018/12/17/42.Supplement_1.DC1/DC_42_S1_Combined_FINAL.pdf Accessed May 2019. 11.Hackett, G et al. J Sex Med. 2018 Apr;15(4):430-457. 12. Lunenfeld et al Recommendations on the diagnosis, treatment and monitoring of hypogonadism in men Aging Male, 2015; 18(1): 5–15

Clinical Efficacy of Testogel® (testosterone) 16.2mg/g Therapy [1,13,14]

1. In a randomised, double-blind, placebo-controlled trial of 274 hypogonadal men, 82.2% achieved serum total testosterone levels within the normal range at day 182, following treatment with Testogel (testosterone) 16.2mg/g gel [13,14]
2. Testogel (testosterone) 16.2mg/g gel is a transparent, colourless gel available in a metered-dose pump, allowing for dose titration, dependent on individual response[1, 13]

Evidence for the Clinical Efficacy of Testogel® (testosterone) 16.2mg/g Therapy: [1,13,14]

1. In a randomised, double-blind, placebo-controlled trial of 274 hypogonadal men, 82.2% achieved serum total testosterone levels within the normal range at day 182, following treatment with Testogel (testosterone) 16.2mg/g gel[13-14]

The primary aim of testosterone therapy is to return testosterone levels of hypogonadal men back to the normal range to alleviate the symptoms of testosterone deficiency.

Kaufman JM et al (2011)[13] initially performed a multicentre, randomised, double-blind placebo-controlled study in hypogonadal men over 182 days to determine the efficacy and safety of Testogel 16.2mg/g vs placebo.

A total of 274 hypogonadal men (234 active; 40 placebo) with average serum total testosterone concentrations <300ng/dL (<10.4nmol/L) took part in the study. All eligible subjects were started at a dose of 2.5g (40.5mg) of 16.2mg/g testosterone gel or matching placebo on day 1 of the study.

Subjects returned to the clinic on Days 14, 28, and 42 for testosterone measurement and the dose was then titrated to either 1.25g, 2.5g, 3.75g or 5.0g accordingly^. Both testosterone gel and placebo gel were applied once daily to either upper arms/shoulders or abdomen[¥]

The primary objective of this study was to demonstrate the efficacy and safety of optimised doses of 16.2mg/g testosterone gel, applied to hypogonadal men over 182 days. The primary statistical objective was to achieve a responder rate of at least 75% in the testosterone gel-treated subjects. Responders were defined as subjects who had average serum testosterone level (C_{av}) in the normal range (300–1,000 ng/dL)^. C_{av} measurements were taken on days 14, 56, 112 and 182.

82.2% of hypogonadal men achieved T levels within the normal range at Day 182, following treatment with Testogel 16.2mg/g. Significantly more subjects receiving titrated doses of testosterone gel at day 182 had testosterone C_{av} values within the normal range vs placebo (p<0.0001). See Table 1.

Table 1:

Number & percentage of subjects achieving Cav target range (300-1000ng/dL)* for testosterone on day 182 following dose titration

Study day	16.2mg/g testosterone gel		Placebo		*P* value
	n/N (%)	95% CI	n/N (%)	95% CI	
182	**139/169 (82.2)**	(75.6, 87.7)	**8/28 (28.6)**	(13.2, 48.7)	<0.0001

Table 1 adapted from Kaufman JM, et al 2011

After titration, the dose distribution was 1.25g (7.3% n=17/234), 2.5g (25.6% n=60/234), 3.75g (28.2% n=66/234), and 5.0g (38.9% n=91/234).

Kaufman JM et al (2012) then carried out a 182-day open-label extension of the previously described pivotal 6-month double-blind efficacy study (Kaufman 2011) to assess the one-year efficacy and safety study of 16.2mg/g testosterone gel in hypogonadal men.

Subjects who completed the initial 182-day portion of the study were eligible to enter the open-label extension for up to 1 year of total participation. At day 182, subjects initially randomised to 16.2mg/g testosterone gel continued on therapy with an opportunity for dose titration, if needed. Formerly placebo subjects were assigned 2.5g testosterone gel and titrated accordingly thereafter.

A total of 191 men comprising of 163 hypogonadal men who continued on testosterone gel from the initial double-blind study and a further 28 men who were formerly on placebo.

The primary efficacy objective was ≥ 75% of subjects from the continuing active group attaining the normal range for total testosterone (Serum Total Testosterone: 300-1000ng/dL)* at final visit (day 364).

On final visit (day 364), 77.9% and 87.0% of patients previously receiving testosterone gel or placebo gel respectively in the previous 6-month double-blind study had C_{av} values within the normal range (300-1000ng/dL)*. See Table 2.

Table 2:

Number & percentage of subjects achieving Cav target range (300-1000ng/dL)* for testosterone on day 364 following dose titration

Study day	Continuing Active		Formerly Placebo		Total (Continuing Active + Placebo)	
	n/N (%)	95% CI	n/N (%)	95% CI	n/N (%)	95% CI
364	**106/136 (77.9)**	70.0, 84.6	**20/23 (87.0)**	66.4, 97.2	**126/159 (79.2)**	72.1, 85.3

Table 2 adapted from Kaufman JM, et al 2012

Based on the last titrated dose (following day 266), final dose allocation to 16.2mg/g testosterone gel was: 1.25g (7.8% n=15/191), 2.5g (21.5% n=41/191), 3.75g (22.5% n=43/191), and 5.0g (48.2% n=92/191).

82.2% and 77.9% of subjects receiving 16.2mg/g testosterone gel for 6 months and 1 year respectively achieved testosterone levels in the normal range thus demonstrating that 16.2mg/g is an effective treatment for achieving normal levels of testosterone in hypogonadal men.

Note: Safety endpoints for Kaufman 2011 and Kaufman 2012 are described in the next section

^ Dose was titrated up or down in 1.25g (20.25mg) increments if total testosterone levels were not within the prespecified range of 350 to 750ng/dL. (12.1 – 26nmol/L)
¥ Application to the abdomen is off license for Testogel 16.2mg/g
*** This equates to 10.4-34.7nmol/L in UK units.**
Note: The normal range in these studies differs from the recent British Society for Sexual Medicine (BSSM) guidelines[5]

2. Testogel (testosterone) 16.2mg/g gel is a transparent, colourless gel available in a metered-dose pump, allowing for dose titration, dependent on individual response[1,13]

- Testogel 16.2mg/g is a transparent, colourless gel available in a metered-dose pump. It is applied to the shoulders or upper arms and does not require daily rotation of the application site.[1]
- 16.2mg/g testosterone gel offers a convenient, flexible and well tolerated dosing regimen that achieved normal testosterone levels in hypogonadal men. [13]
- 16.2mg/g testosterone gel has increased viscosity and provides patients the opportunity to reduce the total mass of gel applied. [13]
- The reduced mass of gel should decrease the overall surface area required for gel application vs. 1% testosterone gel products and may improve patient adherence to treatment.[13]

1. Testogel 16.2mg/g Summary of Product Characteristics, Besins Healthcare, July 2018
https://www.medicines.org.uk/emc/product/8919/smpc Accessed July 2019
5. Hackett G, et al. J Sex Med 2017;14:1504-23
13. Kaufman JM, et al. J Sex Med 2011;8:2079–89.
14. Kaufman JM, et al. J Sex Med 2012;9:1149–61.

Safety Profile of Testogel® (testosterone) 16.2mg/g Therapy [13,14]

1. Studies have shown that Testogel (testosterone) 16.2mg/g is a well-tolerated treatment for male patients with hypogonadism[13,14]

Evidence for the Safety Profile of Testogel® (testosterone) 16.2mg/g Therapy: [13,14]

1. Studies have shown that Testogel (testosterone) 16.2mg/g is a well-tolerated treatment for male patients with hypogonadism[13,14]

Testogel 16.2mg/g is contraindicated:
- in cases of known or suspected prostatic cancer or breast carcinoma[1]
- in cases of known hypersensitivity to testosterone or any other constituent of the gel[1]

Prior to testosterone initiation, 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 must be performed in accordance with recommended methods (Digital rectal examination [DRE] & estimation of serum prostate specific antigen [PSA]) in patients receiving testosterone therapy at least once yearly and twice yearly in elderly patients and at risk patients (those with clinical & familial risk factors). Androgens may accelerate the progression of sub-clinical prostatic cancer and benign prostatic hyperplasia.[1]

The most frequently observed adverse reactions with Testogel 16.2mg/g are as follows:[1]

- Psychiatric disorders - Emotional symptoms (mood swings, affective disorder, anger, aggression, impatience, insomnia, abnormal dreams, increased libido)
- Skin and subcutaneous tissue disorders - Skin reactions (acne, alopecia, dry skin, skin lesions, contact dermatitis, hair colour changes, rash, application site hypersensitivity, application site pruritus).
- PSA increased
- Increased haematocrit or haemoglobin

Patients should wash their hands with soap and water after applying the gel, cover the application area with clothing (such as a sleeved shirt) once the gel has dried and shower/wash the application site(s) thoroughly with soap and water to remove any testosterone residue before any situation in which close contact is foreseen. [1]

Kaufman 2011 - safety endpoints

- All 274 patients who were randomised were included in the safety sample
- Clinical safety was evaluated by recording adverse events and vital signs throughout the study
- In addition, patients received DRE and IPSS-1 assessments on days 84 and 182 to assess prostate safety
- All patients underwent skin application site evaluations using a standardised scale at baseline and at all visits.

They found that a similar percentage of serious treatment-emergent adverse events (TEAEs) occurred in the 16.2mg/g testosterone gel (2.1%) and placebo groups (2.5%).

The percentage of subjects who experienced at least one TEAE during the study was 55.6% (N = 130/234) for the testosterone-treated group vs. 37.5% (n= 15/40) for the placebo group.

Skin irritation assessment indicated no clinically or statistically significant differences between 16.2mg/g testosterone gel and placebo groups. No subject discontinued due to an application site reaction or effect.

The most common adverse event (AE) leading to discontinuation was increased prostate specific antigen (PSA) (PSA >4.0 ng/mL and/or PSA increase from baseline >0.75 ng/mL). which was prespecified in the protocol as a discontinuation criterion.

There were no increases in symptoms of prostatic hypertrophy based on international prostate symptom score (IPSS) results and there were no clinically significant abnormal digital rectal examination (DRE) results.

Kaufman 2012 - safety endpoints

- TEAEs
- Electrocardiograms (ECGs)
- Skin Assessments
- Subjects received follow-up DRE and IPSS assessments on days 266 and 364 to assess prostate safety.

No clinically significant changes in ECGs, IPSS score, or skin irritation assessment were observed.

The percentage of patients with at least one TEAE was 41.4% (79/191) in the testosterone group vs 42.9% (12/28) in the formerly placebo group.

The most common TEAEs in the testosterone group were upper respiratory tract infection (5.2%) and PSA increase* (5.2%).

TEAEs that led to permanent discontinuation of study medication were experienced by 4.7% (9/191) of subjects. The most common of these TEAEs that led to discontinuation was PSA increase*

One patient was discontinued due to a serious adverse event of prostate cancer which was reported as mild and possibly related to study medication.

In conclusion, the authors state that 16.2mg/g testosterone gel for up to 1 year was well tolerated and efficacious, with >77% of patients achieving normal serum testosterone levels following dose titration.

They also conclude that the safety & efficacy profile of the 16.2mg/g testosterone gel appears to be comparable to the 1% testosterone gels used in hypogonadal men however these studies did not directly compare the 2 forms of testosterone gel.

***Average of 2 PSA measurements >4.0ng/ml and/or change from baseline of >0.75ng/ml**

1. Testogel 16.2mg/g Summary of Product Characteristics, Besins Healthcare, July 2018
https://www.medicines.org.uk/emc/product/8919/smpc Accessed July 2019
13. Kaufman JM, et al. J Sex Med 2011;8:2079–89.
14. Kaufman JM, et al. J Sex Med 2012;9:1149–61.

Table 3. Testosterone products indicated for the treatment of male hypogonadism in the UK [3,4]

Testosterone Therapy	Manufacturer
Gels	
Testogel® 16.2mg/g gel pump	Besins Healthcare (UK) Ltd
Testogel® 50mg/5g gel sachets	Besins Healthcare (UK) Ltd
Tostran® 20mg/g gel pump	Kyowa Kirin Ltd Ltd
Testavan® 20mg/g gel pump	Ferring Pharmaceuticals
Injections	
Nebido® 1000mg/4ml	Bayer HealthCare
Sustanon® 250mg/1ml	Aspen Pharma Trading Ltd
Testosterone enantate 250mg/1ml	Alliance Pharmaceuticals
Oral	
Restandol Testocaps® 40mg	Merck Sharpe & Dohme Ltd

Note: Testim although still licensed for use is no longer marketed by Ferring Pharmaceuticals in the UK
https://www.prescriber.org.uk/2018/01/notice-of-testim-discontinuation

Table 4. NHS list price for testosterone products available in the UK [3,4]

Drug Name	Manufacturer	Size	Unit	NHS indicative price
Testogel® 50mg/5g gel sachets	**Besins Healthcare (UK) Ltd**	**30**	**Sachets**	**£31.11**
Testogel® 16.2mg/g gel pump	**Besins Healthcare (UK) Ltd**	**88**	**Grams**	**£31.11**
Tostran® 20mg/g gel pump	**Kyowa Kirin Ltd**	**60**	**Grams**	**£28.63**
Testavan® 20mg/g gel pump	**Ferring Pharmaceuticals Ltd**	**85.5**	**Grams**	**£25.22**
Nebido® 1000mg/4ml	**Bayer HealthCare**	**1**	**Vial**	**£87.11**
Sustanon® 250mg/1ml	**Aspen Pharma Trading Ltd**	**1**	**Ampoule**	**£2.45**
Testosterone enantate 250mg/1ml	**Alliance Pharmaceuticals**	**3**	**Ampoules**	**£87.73**
Restandol Testocaps® 40mg	**Merck Sharpe & Dohme Ltd**	**30**	**Capsules**	**£8.55**

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https://www.prescriber.org.uk/2018/01/notice-of-testim-discontinuation

3. MIMS Online: Accessed June 2019
4. NHS Business Services Authority https://apps.nhsbsa.nhs.uk/DMDBrowser/DMDBrowser.do Accessed June 2019

Table 5. Dosage and frequency of testosterone products in the UK [3,4]

Drug Name	Recommended Dosing
Testogel® 16.2mg/g gel pump	**Apply 40.5 mg transdermally, once daily; increased in steps of 20.25 mg, adjusted according to response; maximum 81 mg per day.**
Testogel® 50mg/5g gel sachets	**Apply 50 mg transdermally, once daily; increased in steps of 25 mg, adjusted according to response; maximum 100 mg per day**
Tostran® 20mg/g gel pump	**Apply 60 mg transdermally, once daily, subsequent application adjusted according to response; maximum 80 mg per day.**
Testavan® 20mg/g gel pump	**Apply 23 mg transdermally, once daily; increased in steps of 23 mg, adjusted according to response; maximum 69 mg per day**
Nebido® 1000mg/4ml	**1g by very slow deep intramuscular (IM) injection into gluteal muscle every 10—14 weeks. Adjust subsequent injection intervals according to serum testosterone levels.**
Sustanon® 250mg/1ml	**Initially, 250mg by slow intramuscular (IM) injection every 2—3 weeks. Maintenance, 250mg by IM injection every 3—6 weeks according to response.**
Testosterone enantate 250mg/1ml	**1ml by deep intramuscular (IM) injection every three weeks.**
Restandol Testocaps® 40mg	**Initially 3—4 oral capsules daily for two to three weeks, adjusting to 1—3 oral capsules daily according to response.**

Note: Testim although still licensed for use is no longer marketed by Ferring Pharmaceuticals in the UK
https://www.prescriber.org.uk/2018/01/notice-of-testim-discontinuation

3. MIMS Online: Accessed June 2019
4. NHS Business Services Authority https://apps.nhsbsa.nhs.uk/DMDBrowser/DMDBrowser.do Accessed June 2019

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