How to successfully administer Nebido®

Information for healthcare professionals

This leaflet provides information on certain aspects of Nebido® administration in order to widen your knowledge on events that might occur during or after the Nebido® injection

Prescribing information can be found on the back cover

NEBIDO®
Testosterone Undecanoate

Nebido® – the long-acting testosterone

Nebido® (testosterone undecanoate, TU) is a long-acting testosterone preparation for the treatment of male hypogonadism confirmed by clinical symptoms and biochemical tests. The intramuscular injection forms a depot from which TU is gradually released. As a result, testosterone levels of the patient will normalise and remain within the normal range for 10–14 weeks.

Check for contraindications and special warnings according to the Product Information/Healthcare Professional Information

Before administering the injection, check the patient for any contraindications: androgen-dependent carcinoma of the prostate or of the male mammary gland; past or present liver tumours; hypersensitivity to the active substance or to any of the excipients. Nebido® is not indicated for use in women.

Nebido® – preparing the injection

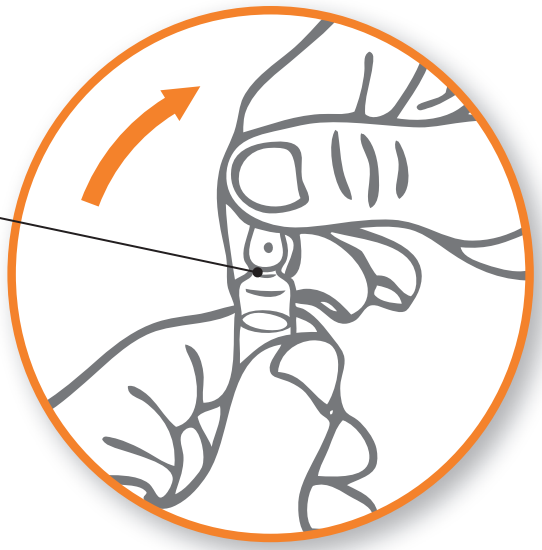
Do not refrigerate

Handling of the ampoule

There is a pre-scored mark beneath the coloured point on the ampoule, eliminating the need to file the neck.

Use both hands to open

While holding the lower part of the ampoule in one hand, use the other hand to break off the upper part of the ampoule in the direction away from the coloured point.



Use a 10ml syringe

10ml syringe

Needle sizes

- To withdraw the solution from the ampoule, use an 18G (1.3mm) needle
- Select the appropriate needle size according to the patient's fat and muscle mass of the gluteal region
- Experts recommend the use of a 20G (0.9mm), 21G [1] (0.8mm) or 22G (0.7mm) needle to ensure a slow intramuscular injection and deposition of Nebido®

Preparation of patient

Relax

Lay the patient down in a comfortable position

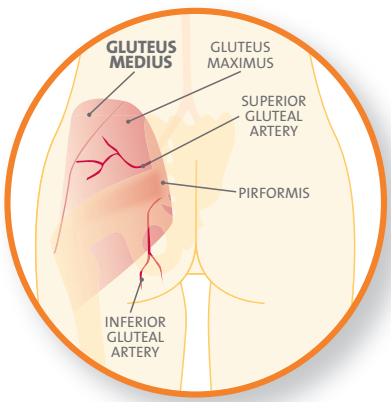
- The deep, intramuscular injection should be administered with the patient lying down
- The bed should be completely flat and the patient's hands should be kept under their head
- You should also remind the patient to remain still during the injection

Performing the injection

At a 90° angle

The preferred site for intramuscular injection is the gluteus medius muscle located in the upper outer quadrant of the buttock.

Care must be taken to prevent the needle from hitting the superior gluteal artery and sciatic nerve. Nebido® should not be split into portions and it should never be administered into the upper arm or the thigh.



The injection process – step-by-step

- As with all oily solutions, Nebido® must be injected strictly intramuscularly and very slowly
- It is recommended to inject Nebido® over approximately 2 minutes
- After selecting the injection site, cleanse the area with an antiseptic
- If there is little muscle mass, you may need to pinch up 2 to 3 edges of the gluteal muscle to provide more volume and tissue to insert the needle
- Insert the needle into the skin at a 90° angle to ensure it is deeply embedded in the muscle
- Grasp the barrel of the syringe firmly with one hand. Using the other hand, pull the plunger back to aspirate for blood
  - If blood appears, do not proceed with the injection. Take the needle out of the patient immediately and replace it
  - Carefully repeat the steps for injection
- If no blood is aspirated, hold the needle position to avoid any movement
- Apply the injection very slowly by depressing the plunger carefully and at a constant rate until all the medication is delivered (ideally over 2 minutes)
- If possible, use your free hand to manually probe or check for depot formation
- Withdraw the needle

The patient should be observed during and immediately after each injection of Nebido® in order to allow for early recognition of possible signs and symptoms which may indicate pulmonary oily microembolism (POME).

Risk management of Nebido®-treated patients

Nebido® – the preparation

Nebido® is an oily solution that contains 1000mg TU dissolved in 4ml castor oil.

As with all oily solutions, Nebido® must be injected strictly intramuscularly and very slowly.

Intramuscular injection of an oil-based preparation requires special care to prevent accidental, direct delivery of the oil-based solution to the vascular system.

Pulmonary oily microembolism

POME is an injection-based reaction and is pathophysiologically related to fat embolism syndrome. It can occur following direct vascular or lymphovascular delivery of oil-based preparations, which then reach the lung from venous circulation and right heart output.

Pulmonary microembolism of oily solutions can in rare cases lead to signs and symptoms such as: cough (or urge to cough), dyspnoea, malaise, hyperhydrosis, chest pain, dizziness, paraesthesia, or syncope.

These reactions may occur during or immediately after the injection and are reversible. Treatment is usually supportive, e.g. by administration of supplemental oxygen.

Sometimes these symptoms may be difficult to distinguish from an allergic reaction which can occur with use of any injectable product.

Suspected anaphylactic reactions after Nebido® injection have been reported.

Recommended treatment schedule

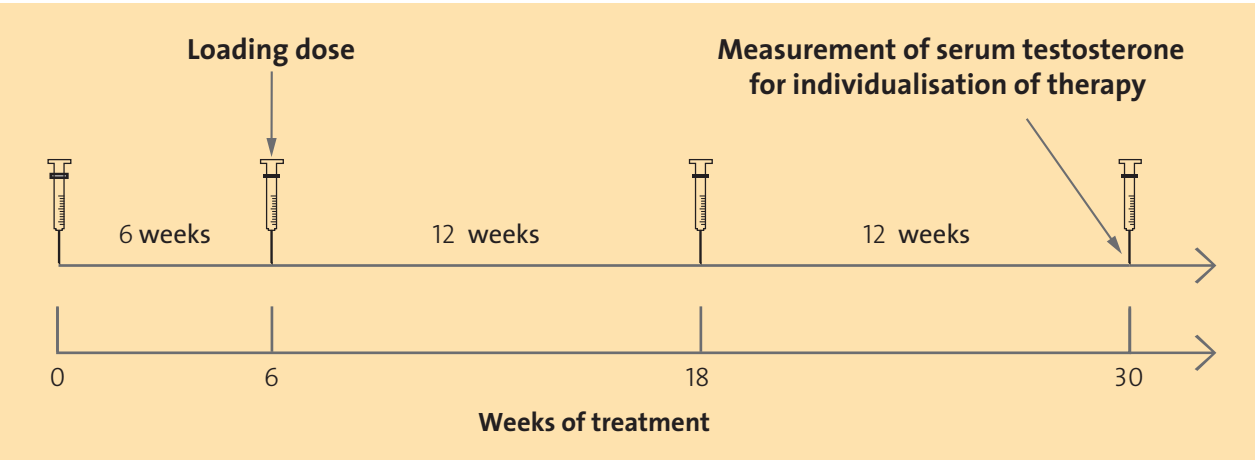
Nebido® is injected in intervals of 10–14 weeks.

Starting treatment

Serum testosterone levels should be measured before start and during initiation of treatment. Depending on serum testosterone levels and clinical symptoms, the first injection interval may be reduced to a minimum of 6 weeks as compared to the recommended range of 10 to 14 weeks for maintenance. With this loading dose, sufficient steady state testosterone levels may be achieved more rapidly.

Maintenance and individualisation of treatment

After this "loading dose", further injections should be given within the recommended range of 10–14 weeks.



Careful monitoring of serum testosterone levels is required during maintenance of treatment. It is advisable to measure testosterone serum levels regularly.

Measurements should be performed at the end of an injection interval and clinical symptoms considered for individualisation of therapy with Nebido®. These serum levels should be within the lower third of the normal range. Serum levels below normal range would indicate the need for a shorter injection interval. In case of high serum levels an extension of the injection interval may be considered.

Safety monitoring during testosterone replacement therapy

Periodic check-ups during long-term androgen therapy are recommended for prostate disease, haemoglobin, haematocrit and liver function tests.

Prostate safety

Prior to initiation of testosterone therapy, all patients must undergo a detailed prostate examination (digital rectal examination and determination of serum PSA) in order to exclude risk of pre-existing prostatic cancer.

After starting testosterone therapy, careful and regular monitoring for prostate disease should be performed in accordance with recommended standard of care methods (digital rectal examination and serum PSA) at 3–6 months, at 12 months and at least annually thereafter (twice yearly in elderly patients and patients at risk).[2]

Haematocrit and haemoglobin

Polycythaemia occasionally develops during testosterone treatment. Therefore, haematological assessment is indicated before treatment, after 3–4 months and 12 months in the first year and then annually thereafter. Dose adjustments may be necessary in case of elevated haematocrit and/or haemoglobin.[2]

Prescribing Information

Nebido® 1000 mg/4 ml, solution for injection (testosterone undecanoate)
Prescribing Information (Refer to full Summary of Product Characteristics (SmPC) before prescribing)

Presentation: 1ml of solution contains 250 mg of testosterone undecanoate, corresponding to 157.9 mg of testosterone. Each 4ml ampoule of solution contains 1000 mg of testosterone undecanoate. **Indication:** Testosterone replacement therapy for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests. **Posology and method of administration:** Strictly for intramuscular use. *Application:* Inject Nebido® extremely slowly. One ampoule (1000mg) is injected intramuscularly every 10 to 14 weeks. Nebido® should be injected deeply into the gluteal muscle, and must be administered very slowly. Special care should be taken to avoid intravasal injection. The contents of an ampoule should be injected intramuscularly immediately after opening the ampoule – refer to the SmPC or PIL for instructions on opening the ampoule safely. *Starting treatment:* Measure serum testosterone levels before the start and during initiation of treatment. If appropriate, first injection interval may be reduced to a minimum of 6 weeks. *Maintenance:* Injection interval within 10 to 14 week range. Monitor serum testosterone and symptoms regularly; adjust injection interval as appropriate. ***Paediatric population:*** Not for use in children. Not evaluated clinically in males under 18. ***Geriatric patients:*** Based on limited data, no dose adjustment is considered necessary. **Contraindications:** Androgen-dependent prostate cancer or breast cancer. Past or present liver tumours. Hypersensitivity to testosterone or any of the excipients. Not for use in women. **Warnings and precautions:** Use only if hypogonadism has been demonstrated and if other etiology has been excluded. Limited experience in patients over 65. Before therapy exclude prostate cancer. Examine prostate and breast at least annually, or twice yearly in elderly or at risk patients (clinical or familial factors). Periodically check testosterone concentrations, haemoglobin, haematocrit and liver function tests. Androgens may accelerate the progression of sub-clinical prostate cancer and benign prostatic hyperplasia. Use with caution in cancer patients at risk of hypercalcaemia (and associated hypercalciuria), due to bone metastases. Regular monitoring of serum calcium concentration is recommended in these patients. Rarely, liver tumours (both benign and malignant) have been reported. Include liver tumour in differential-diagnostic considerations if severe upper abdominal complaints, liver enlargement or signs of intra-abdominal haemorrhage occur. Efficacy and safety of Nebido® has not been demonstrated in patients with hepatic and renal impairment, therefore testosterone replacement therapy should be used with caution in these patients. Nebido® may cause oedema with or without congestive cardiac failure in patients with severe cardiac, hepatic or renal insufficiency, or in patients with ischaemic heart disease. In this case, stop treatment immediately. Use with caution in patients predisposed to oedema, with epilepsy, migraine or blood clotting irregularities. Improved insulin sensitivity may occur. Irritability, nervousness, weight gain, prolonged or frequent erections may indicate excessive androgen exposure requiring dose adjustment. Preexisting sleep apnoea may be potentiated. Testosterone may produce a positive reaction in anti-doping tests. Not suitable for developing muscles or increasing fitness in healthy individuals. Withdraw treatment if symptoms of excessive androgen exposure persist or reappear. **Interactions:** Interactions reported with oral anticoagulants (requires dose monitoring), ACTH or corticosteroids, and thyroxin binding globulin in laboratory tests. **Pregnancy and lactation:** Not for use in women. **Effects on ability to drive and use machines:** None known. **Undesirable effects:** Common – injection site pain, acne, polycythaemia, increased weight, hot flush, increased prostate specific antigen, abnormal prostate examination, benign prostate hyperplasia and various injection site reactions. Serious side effects – *cf. CI/Warnings and Precautions* – in addition, hypersensitivity, cardiovascular disorder, depression, aggression, hypertension, liver function test abnormalities, urinary retention, prostatic intraepithelial neoplasia and prostatitis. Pulmonary microembolism of oily solutions can in rare cases lead to signs and symptoms such as cough, dyspnoea, malaise, hyperhidrosis, chest pain, dizziness, paraesthesia or syncope. Suspected anaphylactic reactions after Nebido injection have been reported. Other side effects - The following adverse reactions have been reported under treatment with testosterone-containing preparations: nervousness, hostility, sleep apnoea, various skin reactions including seborrhoea, increased frequency of erections, in rare cases, priapism, and, in very rare cases, jaundice. Therapy with high doses of testosterone preparations commonly reversibly interrupts or reduces spermatogenesis, thereby reducing the size of the testicles. Prescribers should consult the SmPC in relation to other side effects. **Overdose:** Reduce dose or terminate therapy. **Incompatibilities:** Must not be mixed with other medicinal products. **Legal Category:** POM. **Package Quantities and Basic NHS Costs:** 1 x 4ml ampoule (£80.00). **MA Number(s):** PL00010/0549. **Further information available from:** Bayer plc, Bayer House, Strawberry Hill, Newbury, Berkshire, RG14 1JA, United Kingdom. Telephone: 01635 563000. **Date of preparation:** December 2011.
Nebido® is a trademark of the Bayer Group.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Bayer plc. Tel.: 01635 563500, Fax.: 01635 563703, Email: phdsguk@bayer.co.uk

Date of preparation: May 2012
UK.PH.GM.NEB.2012.011a