How to successfully administer Nebido®

Information for healthcare professionals

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NEBIDO®
Testosterone Undecanoate

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

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 vial

Gloves should be worn while removing the plastic cap on the vial.

Sterilize the rubber membrane

Use an alcohol wipe to sterilize the rubber membrane which is now exposed before withdrawing the medication.

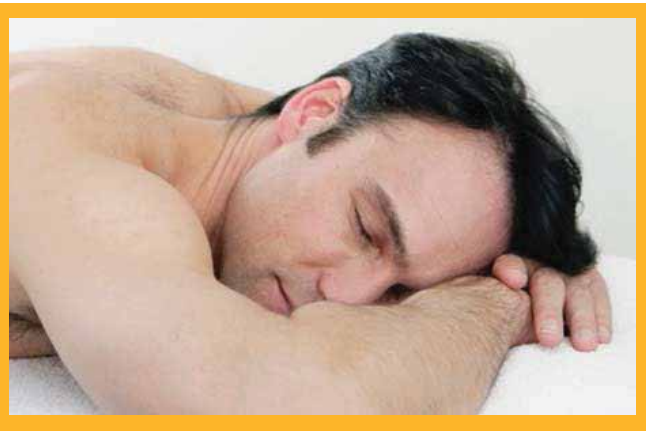
Use a 5ml syringe

5ml
syringe

Needle sizes

- To withdraw the solution from the vial, 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

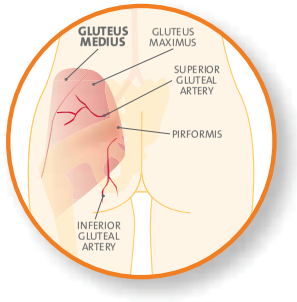
- The deep, intramuscular injection should be administered with the patient lying down
- The bed should be completely flat and the patient's hands should be kept under their head
- You should also remind the patient to remain still during the injection

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, hyperhidrosis, 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

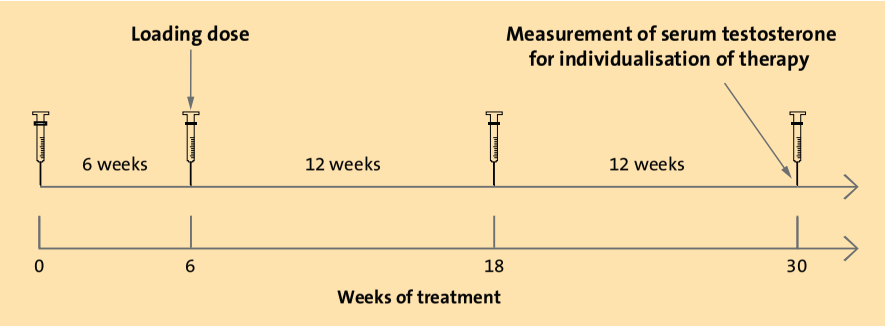
Nebido® is injected in intervals of 10–14 weeks.

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]

Essential Prescribing Information

Nebido® (Testosterone undecanoate) EU Essential Information
Nebido 1000 mg/4 ml, solution for injection. Refer to SmPC (date of revision: November 2012) before prescribing. **Composition:** 4 ml solution containing 1000 mg testosterone undecanoate as active ingredient and benzyl benzoate and castor oil as excipients. **Indications:** Testosterone replacement therapy of confirmed male hypogonadism. **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. Special warnings and precautions: Nebido is not recommended for use in children and adolescents. Nebido is not indicated for use in women. 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 and breast must be performed. The following laboratory parameters should be checked periodically: testosterone, haemoglobin, haematocrit, and liver function tests. Androgens may accelerate the progression of sub-clinical prostatic cancer and benign prostatic hyperplasia. Nebido should be used with caution in cancer patients at risk of hypercalcaemia. Regular monitoring of serum calcium concentrations is recommended in these patients. Benign and malignant liver tumours have been reported in patients receiving testosterone replacement therapy. 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 such case, treatment must be stopped immediately. The limitations of using intramuscular injections in patients with acquired or inherited blood clotting irregularities always have to be observed. Nebido should be used with caution in patients with epilepsy and migraine, as the conditions may be aggravated. Athletes should be advised that Nebido 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. As with all oily solutions, Nebido must be injected strictly intramuscularly and very slowly (over two minutes). 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. These reactions may occur during or immediately after the injection and are reversible. Treatment is usually supportive, e.g. by administration of supplemental oxygen. **Undesirable effects:** Most frequent undesirable effects: acne and injection site pain. Suspected anaphylactic reactions after Nebido injection have been reported. Androgens may accelerate the progression of sub-clinical prostatic cancer and benign prostatic hyperplasia. Other common adverse drug reactions (ADRs): polycythaemia, weight increased, hot flush, prostate specific antigen increased, prostate examination abnormal, benign prostate hyperplasia, injection site reactions (injection discomfort, pruritus, erythema, haematoma, irritation and reaction). Uncommon ADRs: Haematocrit increased, red blood cell count increased, haemoglobin increased, hypersensitivity, increased appetite, glycosylated haemoglobin increased, hypercholesterolaemia, blood triglycerides increased, blood cholesterol increased, depression, emotional disorder, insomnia, restlessness, aggression, irritability, headache, migraine, tremor, cardiovascular disorder, hypertension, dizziness, bronchitis, sinusitis, cough, dyspnoea, snoring, dysphonia, diarrhoea, nausea, liver function test abnormal, aspartate aminotransferase increased, alopecia, erythema, rash, pruritus, dry skin, arthralgia, pain in extremity, muscle disorders, musculoskeletal stiffness, blood creatine phosphokinase increased, urine flow decreased, urinary retention, urinary tract disorder, nocturia, dysuria, prostatic intraepithelial neoplasia, prostate induration, prostatitis, prostatic disorder, libido changes, testicular pain, breast induration, breast pain, gynaecomastia, oestradiol increased, testosterone increased, fatigue, asthenia, hyperhidrosis. 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. Other known ADRs of testosterone-containing preparations: nervousness, hostility, sleep apnoea, various skin reactions including seborrhoea, increased frequency of erections, rare cases of persistent, painful erections (priapism), in very rare cases jaundice. Therapy with high doses of testosterone commonly reversibly interrupts or reduces spermatogenesis, thereby reducing the size of the testicles. High-dosed or long-term administration of testosterone occasionally increases the occurrences of water retention and oedema. **Posology and method of administration:** Nebido is injected every 10 to 14 weeks. Nebido is strictly for intramuscular injection and must be administered very slowly (over two minutes). Care should be taken to inject Nebido deeply into the gluteal muscle following the usual precautions for intramuscular administration. Special care must be taken to avoid intravasal injection. The first injection interval may be reduced to a minimum of 6 weeks. Nebido is not indicated for use in children and adolescents and it has not been evaluated clinically in males under 18 years of age. **Legal Category:** Medicinal product subject to medical prescription. **Marketing Authorisation holder:** Bayer Pharma AG, 13353 Berlin, Germany. For further details contact your local Bayer Pharma organisation. **Version:** 16 July 2012.

References
1. Sartorius *G et al. Asian J Androl* 2010;12(2):227–233.
2. Wang *C et al. Eur Urol* 2009;55:121–130.

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Any suspected adverse drug reactions can be reported to:
Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens,
Gżira GŻR 1368, MALTA,
or at:
http://www.medicinesauthority.gov.mt/adrportal Telephone Number: +356 2343 9000
Or
Alfred Gera & Sons Ltd, Triq il-Masġar, Qormi QRM 3217, MALTA,
or at:
pv@alfredgera.com Telephone Number: +356 21446205