

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Nebido®

Solution for injection



One vial contains:
1000 mg testosterone undecanoate
(1 ml solution for injection contains 250 mg testosterone undecanoate, corresponding to 157.9 mg testosterone).
Inactive ingredients and allergens: see section 6 "Further Information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1) WHAT IS THE MEDICINE INTENDED FOR?

Nebido is intended for use in adult men as a testosterone replacement to treat problems caused by a testosterone deficiency (male hypogonadism). Testosterone deficiency will be confirmed by two separate blood testosterone measurements and will also include clinical symptoms such as:

- impotence
- infertility
- low sex drive
- tiredness
- depressive moods
- loss of bone mass caused by low hormone levels

Nebido is slowly injected into the muscle, there it is stored and gradually released over a period of time.

Therapeutic group: Nebido is a replacement for the male hormone (androgen) testosterone, and belongs to a group of medicines called androgens.

2) BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to testosterone undecanoate or to any of the other ingredients contained in the medicine. For a list of the inactive ingredients, see section 6 "Further Information".
- You have an androgen-dependent cancer or suspected cancer of the prostate or of the breast.
- You have or had a liver tumor.
- You are a woman.

Special warnings regarding use of the medicine

Before using Nebido tell your doctor if you are suffering, or have suffered in the past, from:

- Epilepsy
- Heart, kidney or liver problems
- Migraine
- Temporary interruptions in your breathing during sleep (apnea), as these may get worse
- Cancer, as the level of calcium in your blood may need to be tested regularly
- High blood pressure, or if you are being treated for high blood pressure, as testosterone may cause a rise in blood pressure
- Blood clotting problems
 - bleeding disorders (that is, hemophilia)
 - thrombophilia (an abnormality of blood coagulation that increases the risk of thrombosis - blood clots in blood vessels).
 - factors that increase your risk for blood clots in a vein: previous blood clots in a vein; smoking; obesity; cancer; immobility; if one of your immediate family has had a blood clot in the leg, lung or other organ at a young age (e.g., below the age of about 50); or as you get older.

How to recognise a blood clot: painful swelling of one leg or sudden change in colour of the skin, e.g., turning pale, red or blue, sudden breathlessness, sudden unexplained cough which may bring up blood; or sudden chest pain, severe light headedness or dizziness, severe pain in your stomach, sudden loss of vision. Seek urgent medical attention if you experience one of these symptoms.

There have been reports of thrombotic events (e.g. deep-vein thrombosis, pulmonary embolism, ocular thrombosis) during testosterone therapy in thrombophilia patients. In thrombophilia patients, there have been reports of blood clots even under anticoagulation treatment; therefore, continuing testosterone treatment should be carefully evaluated after the first thrombotic event. In case of treatment continuation, further measures should be taken to minimize the risk of formation of blood clots.

Nebido is not intended for use in children and adolescents under 18 years of age.

Tumors

Androgens may accelerate the progression of prostate cancer and benign prostatic hyperplasia

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

Cases of benign and malignant liver tumors have been reported in users of hormonal substances such as androgens. If severe upper abdominal complaints, liver enlargement or signs of intra-abdominal hemorrhage occur in men using Nebido, a liver tumor should be included in the diagnostic considerations.

If you are suffering from severe heart, liver or kidney disease, treatment with Nebido may cause severe complications manifested by water retention in your body sometimes accompanied by heart failure.

The following blood tests have to be performed by your doctor before and during treatment: blood testosterone level, full blood count.

If your liver is not functioning properly

No formal studies have been performed in patients with liver impairment. You will not be prescribed Nebido if you have ever had a liver tumor (see section 2 "Do not use the medicine").

Elderly patients (65 years or older)

There is no need for your doctor to adjust the dose if you are over the age of 65 (see below "Tests and follow-up").

There is limited experience on the safety and efficacy of the use of Nebido in patients over 65 years of age. It should be taken into account that physiological testosterone serum levels decline with increasing age.

Muscle building and drug tests

Nebido is **not** suitable for building muscles in healthy individuals or for increasing physical strength. Nebido might lead to positive results in drug tests.

The effects of drug abuse and development of dependence
Always take the medicine precisely as instructed by the doctor or pharmacist.

Testosterone abuse, especially when taking more than the recommended dose, alone or in combination with another anabolic androgenic steroid, can lead to serious medical problems in your heart and blood vessels (which can be fatal), mental problems and/or hepatic problems. People who abused testosterone can develop dependence and can experience withdrawal symptoms upon significant dosage reduction or abrupt discontinuation of use. Do not abuse this medicine or its combination with another anabolic androgenic steroid, since such use is very dangerous to your health (see section 4 "side effects").

Children and adolescents

The medicine is not intended for children and adolescents under the age of 18.

There is no information on the use of Nebido in males under the age of 18.

Tests and follow-up

Male hormones may increase the development of prostate cancer and enlarged prostate gland (benign prostatic hypertrophy). Before your doctor injects Nebido, he/she will examine you to make sure that you do not have prostate cancer.

Your doctor will regularly examine your prostate and breast, especially if you are elderly. He/She will also take regular blood samples.

Following the use of hormonal substances such as androgen compounds, cases of benign (non-cancerous) and malignant (cancerous) liver tumors have been observed.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. You must also inform the doctor or pharmacist if you are likely to start taking any other medication. Especially if you are taking:

- The hormone ACTH or corticosteroids (used to treat various conditions such as rheumatism, arthritis, allergic conditions and asthma): Nebido may increase the risk of water retention, especially if your heart and liver are not functioning properly
- Blood-thinning tablets (coumarin derived oral anticoagulants), since they could increase the risk of bleeding. Your doctor will check the dose.
- Medicines to treat diabetes. It may be necessary to adjust the dose of your blood sugar reducing medicine. Like other androgens, testosterone may increase the effect of insulin. It is possible that the doctor will adjust the dosage of Nebido if you are taking one of these medications.

Please be sure to inform your doctor if you suffer from a disturbance in blood clotting, as it is important for your doctor to know this before deciding to inject Nebido.

Nebido may also affect the results of some laboratory tests (e.g., thyroid gland). Tell your doctor that you are using Nebido.

Pregnancy, breastfeeding and fertility

Pregnancy and breastfeeding:

Nebido is not intended for use in women and must not be used in pregnant or breastfeeding women.

Fertility:

Treatment with high doses of testosterone preparations may commonly but reversibly stop or reduce sperm production (see also section 4 "Side effects").

Driving and using machines

No effect of Nebido on your ability to drive or use machines has been observed.

Important information regarding some of the ingredients of the medicine

Nebido contains benzyl benzoate. Nebido contains 2000 mg benzyl benzoate in each 4 ml vial, which is equivalent to 500 mg/ml.

3) HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Check with your doctor or pharmacist if you are uncertain regarding dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

The usual dosage is generally: one injection (1 vial) every 10 to 14 weeks.

This dosage is enough to maintain a sufficient testosterone level without leading to a build-up of testosterone in the blood.

Do not exceed the recommended dose.

Mode of administration:

Your doctor will inject Nebido (1 vial) very slowly into a muscle. Nebido is intended for intramuscular injection only. Special care must be taken to avoid injection into a blood vessel (see "Administration of the injection").

Start of treatment

Your doctor will measure your blood testosterone levels before starting treatment and during the early stages of treatment. It is possible that your doctor may give you the second injection after only six weeks in order to quickly attain the necessary testosterone level.

This will depend on your symptoms and testosterone levels.

Maintaining Nebido levels during treatment

The injection interval should always be within the recommended range of 10 to 14 weeks.

Your doctor will measure your testosterone levels regularly at the end of an injection interval to make sure they are at the appropriate level. If the level is too low, your doctor may decide to give you injections more often.

If your testosterone levels are high, your doctor may decide to give you injections less often.

Do not miss your injection appointments. Otherwise, your optimum level of testosterone will not be maintained.

If you think that the effect of Nebido is too strong or too weak, tell your doctor.

If you accidentally took a higher dosage than recommended, the following symptoms may occur:

- restlessness
- nervousness
- weight gain
- long-lasting or frequent erections

Tell the doctor if you suffer from any of the conditions mentioned above. Your doctor will inject you less often or will stop the treatment.

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

Adhere to the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take the medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4) SIDE EFFECTS

As with any medicine, use of Nebido may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

The most common side effects are acne and pain at the injection site.

Common side effects (may affect up to 1 in 10 users):

- abnormally high levels of red blood cells
- weight gain
- hot flushes
- acne
- enlarged prostate gland and associated problems, prostate-specific antigen increased, prostate examination abnormal, benign prostate hyperplasia
- various reactions at the injection site (e.g., pain, bruising, or irritation)

Uncommon side effects (may affect up to 1 in 100 users):

- allergic reaction
- increased appetite, changes in blood test results (e.g., increased blood sugars or fat levels)
- depression, emotional disorder, insomnia, restlessness, aggression, or irritability
- headache, migraine, or tremor
- cardiovascular disorder, high blood pressure, or dizziness
- bronchitis, sinusitis, cough, shortness of breath, snoring, or voice problems
- diarrhea, or nausea
- changes in liver test results, aspartate aminotransferase levels increased
- hair loss, or various skin reactions (e.g., rash, itching, redness or dry skin)
- joint pain, pain in limbs, muscle problems (e.g., spasm, pain or stiffness), or an increase in creatine phosphokinase in the blood
- urinary tract disorders (e.g., decreased flow of urine, urinary retention, urge to urinate at night, dysuria)
- prostate disorders (e.g., prostatic intraepithelial neoplasia, or hardening or inflammation of the prostate gland), changes in sexual desire, painful testicles, painful, hardened or enlarged breasts, or increased levels of male and female hormones
- tiredness, general feeling of weakness, increased sweating, or night sweat

Rare side effects (may affect up to 1 in 1000 users):

The oily liquid Nebido may reach the lungs (pulmonary microembolism of oily solutions), which in rare cases could cause signs and symptoms such as cough, shortness of breath, feeling generally unwell, excessive sweating, chest pain, dizziness, numb sensation ("pins and needles"), or fainting. These reactions may occur during or immediately after the injection, and are reversible.

Suspected anaphylactic reactions after Nebido injection have been reported.

Androgens may accelerate the progression of prostate cancer and benign prostatic hyperplasia

In addition to the side effects listed above, the following reactions have been reported following treatment with preparations containing testosterone: nervousness, hostility, brief interruptions in breathing during sleep, various skin reactions including dandruff and oily skin, increased hair growth, more frequent erections, and very rare cases of yellowing of the skin and eyes (jaundice).

Treatment with high doses of testosterone preparations commonly stops or reduces sperm production, thereby reducing the size of the testicles, although this returns to normal after cessation of treatment. Testosterone replacement therapy in cases of low functioning testicles (hypogonadism) can, in rare cases, cause persistent, painful erections (priapism). High doses or long-term administration of testosterone occasionally increase cases of water retention and edema (swelling due to fluid retention).

For testosterone preparations in general, a common risk of increased red blood cell count, increased hematocrit (percentage of red blood cells in blood) and hemoglobin (the component of red blood cells that carries oxygen), were observed in periodic blood tests.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

5) HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Store at a temperature below 30°C.
- The vial must be used immediately after opening.
- The preparation may only be used if it is clear and particle-free.
- Do not discard medicines into the wastewater or household waste. Ask the pharmacists how to dispose of medicines no longer in use. These measures will help protect the environment.

6) FURTHER INFORMATION

- In addition to the active ingredient, testosterone undecanoate, the medicine also contains:
 - Benzyl benzoate, castor oil refined.
- What does the medicine look like and what are the contents of the package?
Nebido is a clear, yellowish, oily liquid. The preparation comes in a package of one brown glass vial containing 4 ml of solution for injection.
- Registration Holder and address: Bayer Israel Ltd., 36 Hacharash St., Hod Hasharon 45240.
- Manufacturer and address: Bayer AG, Berlin, Germany.
- Revised in March 2021 according to MOH guidelines
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 134 77 31162 11

The following information is intended for the medical staff only:

At low storage temperatures the properties of this oil-based solution will temporarily change (e.g., higher viscosity, cloudiness). If the preparation is stored at a cold temperature, the product should be brought to room temperature or body temperature before use.

Before use, the solution for intramuscular injection should be visually inspected and only clear solutions free from particles should be used.

The contents of a vial should be injected intramuscularly immediately after opening the vial.

The medicinal product is for a single use only and any remaining unused solution should be discarded.

Administration of the injection

Special care must be taken to avoid injection into a blood vessel.

As with all oily solutions, Nebido must be injected directly into the muscle only and very slowly. Pulmonary microembolism of oily solutions can in rare cases lead to a sign and symptoms such as cough, shortness of breath, general unwell feeling, excessive sweating, chest pain, dizziness, paraesthesia or fainting. These reactions may occur during or immediately after the injection and are reversible. Treatment is usually supportive, e.g., administration of supplemental oxygen.

Suspected anaphylactic reactions after injection of Nebido have been reported.

Warnings

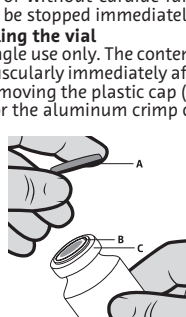
Careful and regular monitoring of the prostate gland and breasts must be performed in accordance with recommended methods at least once yearly (digital rectal examination and measurement of serum PSA) in patients receiving testosterone therapy, and twice a year in elderly patients and patients at risk (those with clinical or familial factors).

Besides laboratory tests for testosterone concentrations in patients on long-term androgen therapy, the following laboratory tests should be performed periodically: hemoglobin, hematocrit, and liver function tests and lipid profile.

In patients suffering from severe cardiac, hepatic or renal insufficiency or ischemic heart disease, treatment with testosterone may cause severe complications characterized by edema with or without cardiac failure. In such a case, treatment must be stopped immediately.

Notes on handling the vial

The vial is for single use only. The contents of the vial must be injected intramuscularly immediately after drawing it into the syringe. After removing the plastic cap (A), do not remove the metal ring (B), or the aluminum crimp cap (C).



NEBI SOL PL SH 100621



88252152

