# Testosterone undecanoate (Nebido®) for the indication 'hypogonadism'
# Pharmacotherapeutic report, summary

Approved on 26 November 2012 by the Medicinal Products Reimbursement Committee (CFH)

**Medicine.** Testosterone undecanoate (1000 mg/4 ml, solution for injection)

**Registered indication.** "Testosterone replacement therapy for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests."

**Posology.** 1000 mg i.m. per 10-14 weeks

**Mechanism of action.** Testosterone undecanoate (TU) is an ester of naturally occurring andogen, testosterone. The active form, testosterone, is formed by cleavage of the side chain. After injection, the compound is gradually released from the depot and is almost completely cleaved by serum esterases into testosterone and undecanoic acid.

**Specific details.** Testosterone undecanoate is also available as an oral (capsule) medicine for the treatment of hypogonadism. Nebido should only be used if hypogonadism (hyper- and hypogonadotrophic) has been demonstrated and if other aetiology, responsible for the symptoms, has been excluded before treatment is started. Testosterone insufficiency 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 two separate blood testosterone measurements. The application relates only to the classic forms of hypogonadism, and not to administration for 'late onset' hypogonadism.


**Summary of the therapeutic value**

**Intended effects**. The efficacy of i.m. TU in terms of normalising the physiological range of testosterone concentrations has been sufficiently demonstrated. It is not possible to demonstrate clinically relevant differences between different products in controlling symptoms related to the stability of testosterone levels within the physiological range on the basis of the indirect comparisons. There is no direct comparative, double-blind study of sufficient quality and size and with a sufficient follow-up on efficacy or improvement of clinical symptoms, with validated outcome measures such as quality of life, of i.m. TU versus other products available in the Netherlands. Neither has relevant placebo-controlled research of i.m. TU been carried out regarding the above-mentioned aspects. This means that, as far as intended effects are concerned, insufficient evidence is available to be able to conclude that a clinically relevant difference exists between the various testosterone products.

**Unintended effects**. The most frequently reported unintended effects of testosterone supplementation are based on the androgenic working of testosterone and include prostate disorders (including benign prostate hyperplasia and increased PSA), polycytemia, acne and hypertension. These systemic unintended effects do not differ substantially between the various products. Unintended effects at the injection side may occur, depending on the means of administration.

**Experience**. Sufficient experience has been obtained with testosterone undecanoate i.m., and ample experience has been obtained with testosterone gel, oral TU and Sustanon®.
**Applicability**. There are no major differences in applicability between i.m. testosterone undecanoate and the other administrative forms of testosterone.
**Ease of use**. The ease of use of i.m. testosterone undecanoate is greater than that of Sustanon® due to the longer interval between injections, but the ease of use of i.m. testosterone undecanoate in comparison with other forms of administration depends on patients' preferences.

**Final conclusion.** Based on the available pharmacokinetic research, the intended effects of i.m. testosterone undecanoate, based on obtaining a physiological testosterone serum level, can be regarded as equivalent of those of testosterone gel, oral testosterone undecanoate and Sustanon®. Insufficient research of a sufficient quality is available to be able to demonstrate intended and unintended effects of i.m. testosterone undecanoate in comparison with other products commonly used in the Netherlands on men with hypogonadism. The ease of use of i.m. testosterone undecanoate is greater than that of Sustanon® because it is administered less frequently, but there is no evidence that this leads to improved therapy compliance and as a result to more favourable outcomes.

When treating hypogonadism, the therapeutic value of i.m. testosterone undecanoate is equal to that of the other testosterone products available in the Netherlands.

*The original text of this **CFH-Report** of CVZ was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of CVZ's CFH-Report.*
*Furthermore, CVZ points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.*