



## 1. Medical Condition

### MALE HYPOGONADISM

## 2. Diagnosis

### A. Medical history

The etiology of hypogonadism must be clearly identified:

- **Primary hypogonadism** (e.g. Klinefelter syndrome, bilateral anorchia, cryptorchidism, Leydig cell aplasia, male Turner syndrome, Noonan's syndrome, congenital adrenal hyperplasia)
- **Or secondary hypogonadism** (e.g. panhypopituitarism, idiopathic hypogonadotropic hypogonadism, Kallmann's syndrome, constitutional delay of puberty, LH deficiency, Prader Willi syndrome)

### B. Diagnostic criteria

- Clinical history with **biological assays** of testosterone, LH and FSH, confirming the diagnosis must be presented. The obtained values must be interpreted by an endocrinologist or specialist in internal medicine.
- Appropriate **stimulation of the gonadal axis** by hCG and results should be provided.

### C. Relevant medical information

In cases of traumatic hypogonadism (bilateral anorchia) surgical evidence or imaging should be provided when possible.

### 3. Medical best practice treatment

#### A. Name of prohibited substance

Enanthate testosterone or cypionate testosterone

#### B. Route

1. Testosterone will be preferably administered by regular intramuscular injection. The treatment must be recorded by a health professional and kept available for control at any time. The use of transdermal testosterone skin patches could be an alternative to consider based on specialist advice. For medical reasons (hepatocellular risks) oral androgens should not be used.

2. The administration of testosterone will be conducted **by IM injection every two to four weeks** to replace endogenous secretion.

#### C. Frequency

1. The dosage must be decided by at least one endocrinologist or internal medicine experienced physician and confirmed by appropriated serum measures in relation to injection times. The age-related normal range for testosterone serum levels must always be respected. Permanent high levels (levels should normalise in the two days following injection) and over replacement should never been accepted.

2. The reference dosage is from 50 to 250 mg cypionate testosterone by IM every two weeks or enanthate testosterone every three to four weeks to replace endogenous secretion.

#### D. Recommended duration of treatment

The treatment may be for life but an annual review including evidence of well-controlled therapy must be provided.

### 4. Other non-prohibited alternative treatments?

If the diagnosis is confirmed there is no non-prohibited alternative treatment.

## 5. Consequences to health if treatment is withheld

Serious impairment.

- Under developed genitals (if before puberty)
- Muscle weakness
- Serious osteoporosis
- Diminished libido
- Erectile dysfunction /impotence
- Male infertility
- Depression

## 6. Treatment monitoring

Frequent and unannounced serum testosterone measures should be imposed and related to the injection period or patch application.

## 7. TUE validity and recommended review process

The duration of approval will be limited in all cases to 3 years at a maximum. In all cases an annual review process with a control of well adapted dose should occur each year. Another independent specialist may be consulted as necessary.

## 8. Any appropriate cautionary matters

- Oral androgens should not be used for medical reasons.
- In the particular case of a young athlete with delayed puberty the opinions of a pediatrician and an endocrinologist must confirm the diagnosis and a need for testosterone supplementation. This should be accompanied by the report of a relevant clinical examination. The approval must always be for a period of no more than one year.
- Given the potential controversy associated with the approval of a TUE for testosterone the opinion of an independent expert is strongly recommended.

## 9 References

1. The Merck Manual, sec 19, Ch. 269, Endocrine and metabolic disorders
2. The American Association of Clinical Endocrinologists "2002 update guidelines for evaluation and treatment of hypogonadism in adult male patients"
3. Rhoden EI, Morgentaler A. Risks of testosterone replacement therapy and recommendations for monitoring. *New Eng J Med* 2004; 350:482-92
4. Vermeulen A, Kaufman JM. Ageing of the hypothalamo-pituitary-testicular axis in male. *Horm Res.* 1995; 43:25-28