Testosterone (Sustanon®injection and Tostran® gel) in male children and adolescents

Traffic light classification - Amber 1
Information sheet for Primary Care Prescribers

Licensed Indications

Sustanon-250 injection is licensed for testosterone replacement therapy and should be used with caution in children.

Tostran 2% gel is licensed in adults for testosterone replacement therapy, but not licensed in children.

The British Society for Paediatric Endocrinology and Diabetes (BSPED) recommend several licensed preparations for use off-label in children.

This information sheet covers use for the following indications

- Constitutional delay in growth and puberty (CDGP)
- Hypogonadism

Products should only be used when testosterone deficiency has been confirmed by clinical features and biochemical tests.

Exclusions

- Patients who have not completed a specialist assessment and evaluation to confirm diagnosis of CDGP or Hypogonadism
- Female patients
- Children under 3 years

Therapeutic Summary

The aim of testosterone replacement therapy is to mimic the normal cadence of puberty and match requirements at different stages of pubertal development in patients with Hypogonadism and CDGP. Testosterone replacement therapy is used to induce development of secondary sexual characteristics and promote linear growth, normal accrual of muscle mass and bone density while avoiding premature epiphyseal plate closure. Testosterone replacement therapy is usually started from the age of 12-14 years and dose is reviewed 6 monthly increasing progressively over 24-36 months until adult maintenance dose is reached. The maintenance dose of testosterone replacement is continued into adult life. In the case of CDGP the testosterone is stopped when there is established endogenous puberty, as assessed by the specialist.

All boys with delayed puberty (absence of signs of secondary sexual development i.e. testicular volume less than 4 mL at 14 years of age) should be referred to paediatric endocrinology for assessment. CDGP is the most common cause but it can be extremely difficult in the early stages of puberty to differentiate CDGP from Hypogonadism. Boys with CDGP/Hypogonadism may manifest with psychological distress because of their lack of growth and pubertal progression, which can affect their school performance, social

relationships and can affect their psychological wellbeing. A course of testosterone treatment should be offered in order to enhance growth rate and expedite the features of puberty. In those with CDGP who receive testosterone treatment, the intervention is well tolerated, highly effective and regarded as a standard therapeutic option.

Monitoring of growth and pubertal status is paramount in boys who receive testosterone replacement treatment. This is done by the paediatric endocrine specialist team every 6 months.

Medicines Initiation

Testosterone replacement therapy for pubertal induction in children and adolescents will only be started in primary care following recommendation from paediatric consultant endocrinologist.

Products available, dosages, route of administration and duration

Table 1: Testosterone delivery for constitutional delay in growth and puberty

	Intramuscular (preferred option)	**Metered-dose gel (secondary option)**
Preparation	Testosterone Proprionate. Sustanon-250® (250mg/ml ampoule for injection)	Tostran® (2%; 10mg testosterone per metered application)
Initial dose	50mg-100mg (0.2ml -0.4ml)	10-20mg
Frequency	Monthly	Once daily
Duration	3-6 months	3-6 months

Table 2: Testosterone delivery for pubertal induction in boys with hypogonadism:

	Intramuscular (preferred option)	**Metered-dose gel (secondary option)**
Preparation	Testosterone Proprionate. Sustanon-250® (250mg/ml ampoule for injection)	Tostran® (2%; 10mg testosterone per metered application)
Initial dose	50mg-100mg (0.2ml-0.4ml)	10-20mg
Initial Frequency	Monthly	Once daily
Titration	Increase by 50mg (0.2ml) every 6-12 months, increasing frequency to 2-3 weekly once 250mg reached	Increase by 10mg every 6 months
Adult dosing	200-250mg 2-4 weekly	60-80mg once daily

In the treatment of hypogonadism, dose escalation to achieve adult dosing of 250mg every 3 weeks may take 2.5 years to 3 years to be established. This group of boys will be reviewed

in the transitional clinic for joint review with adult endocrinologist. Information will be provided on other testosterone preparations once maintenance dose is established. Testosterone replacement information sheet for male hypogonadism in adults can be located here

Health care practitioners can follow the Sustanon-250® intramuscular injection administration guide in paediatrics.

Duration of treatment

Patients with a diagnosis of CDGP will mostly complete the course at 6 months, rarely requiring treatment beyond 12 months.

Patients with a diagnosis of hypogonadism will require life-long treatment with testosterone replacement therapy.

Monitoring Requirements and Responsibilities

All monitoring will be done in secondary care.

Table 3: Assessments to be taken in secondary care specialist clinic.

	3-6 monthly	12 monthly
Pubertal development and staging	✓	
Height and weight	✓	
Bone age		✓

The local specialist team have advised that further monitoring will not be required by primary care as the doses for pubertal induction are so much lower than the normal doses used for testosterone replacement.

Explicit criteria for review and discontinuation of the medicine

In patients with CDGP, keep under specialist review until testicular volumes are 10mL or more. If during treatment for hypogonadism, an increase in testicular volume is noticed, treatment must be discontinued immediately and diagnosis reviewed. Treatment can be recommenced once diagnosis of hypogonadism due to testicular failure is reconfirmed.

Contraindications

- Hypersensitivity to the active substance or to any of the excipients in any of the testosterone formulations i.e. Arachis oil in Sustanon-250
- Known or suspected carcinoma of the prostate or breast.

Precautions

- Sustanon®-250 contains arachis oil and therefore should be used with caution in those with peanut allergy (and soya allergy, due to cross sensitivity). The arachis oil does not

contain peanut protein and therefore most individuals with peanut allergy will tolerate the preparation, unless their sensitivity is high.

- Care and clarity must be taken when prescribing volumes of testosterone intramuscular injection. The recommendation is to write dose and volume on prescriptions e.g. "Sustanon® 250mg/ml injection: administer 50mg (0.2ml of 250mg/ml vial) IM monthly". This dosage direction must also be clear on the written communication to primary care practitioners.
- With topical formulations men should avoid skin to skin contact with pregnant or breastfeeding women. During application, female carers should be advised to wear gloves. In the event of contact the area of the skin should be washed with warm soapy water as soon as possible.
- Topical formulations must specify form i.e. gel to avoid prescriptions for cream, which can cause variations in dosing.

Side-effects

Local discomfort at injection site due can occur due to the oily formulation. The injection site should be varied periodically to minimise this.

Other side-effects include: priapism, polycythaemia, electrolyte imbalance, fluid retention, depression, altered mood, nervousness, pruritus, acne, weight gain, sleep apnoea, hypertension, cholestatic jaundice.

Clinically relevant medicine interactions and their management

- Phenobarbitone may increase the rate of metabolism of testosterone
- Testosterone may enhance the activity of coumarin anticoagulants and oral hypoglycaemic agents.
- Testosterone may decrease concentrations of thyroxine-binding globulin, resulting in decreased T4 serum concentrations and increased uptake of T3 and T4.

Information given to patient

Advice to patients/carers:

- Female carers must be advised to wear gloves to avoid cross transfer of Tostran® gel
- Attend all follow-up appointments and participate in monitoring requirements.

Further advice and support – this information is not inclusive of all prescribing information
Summary of products characteristics via electronic Medicines Compendium (eMC) British National Formulary for children via www.medicinescomplete.com Consultant Paediatric Endocrinologists Secretary Telephone Number: 0115 924 9924 Ext 62336 Paediatric Endocrine Specialist Nurse Telephone number: 0115 924 9924 Ext 85123 Paediatric Pharmacy Team Telephone Number: 0115 924 9924 Ext 64410

Specialist Contact Details (out of hours)

For Medical Professionals – Ring 0115 924 9924 and ask to speak to the Paediatric Endocrinology Consultant on call.

For Patients – Ring 0115 924 9924 and ask to speak to on call paediatric medical registrar.

Acknowledgements

Adapted from Leicestershire medicines strategy group shared care agreement for children and adolescents for induction of and progression through puberty in hypo-gonadotrophic hypogonadism (HH), hypogonadism due to primary testicular failure (PTF) and in constitutional delay of growth and puberty (CDGP).

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