FULL SHARED CARE AGREEMENT FOR

Testosterone replacement therapy in children and adolescents for induction of and progression through puberty in hypogonadotrophic hypogonadism (HH), hypogonadism due to primary testicular failure (PTF) and in constitutional delay of growth and puberty (CDGP)

Sharing of care assumes communication between the specialist, GP and patient, and other members of the care team including specialist nurses and pharmacists. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

If a GP is invited by the specialist to participate in a shared care arrangement, the GP should reply to this request within 10 working days. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

Specialist responsibilities

1. Diagnosis of condition and ensuring other treatment options have been fully explored. The consultant will recommend commencing testosterone and will provide the GP with a full report justifying testosterone therapy.
2. State place in therapy and confirm if there is a specific patient selection e.g. patients who have failed on other therapies.
3. Baseline FBC, LFTs, lipids, LH, FSH and testosterone levels.
4. Initiation of treatment, inform GP of ongoing schedule and respond to any queries and provide advice during the treatment.
5. Arrange for the first injection to be given by the endocrine clinic specialist nurse in hospital.
6. Advise GP on monitoring for response and adverse drug reactions (ADRs) during initiation period.
7. Liaison with the GP to share the patient’s care when a stable dose has been achieved and proven benefit has been established using the Shared Care Request Form: Shared Care Request Form. Shared care should not be assumed until a written agreement has been received from the GP.
8. Review associated drug therapy.
9. Review patient’s pubertal development, growth and response to treatment at 3 to 6 monthly intervals. Monitoring will include height and weight measurements, pubertal staging, bone age assessment at approximately 12 monthly intervals, and hormone measurements as indicated.
10. If appropriate, discharge patient and clearly outline to GP when therapy may be reduced and stopped assuming no relapse in patient’s condition. Review periods to be agreed.
11. Respond to issues raised by GP after care of patient has been transferred.
12. Advise GP on related issues such as drug interactions - phenobarbitone may increase the rate of metabolism of testosterone; testosterone may enhance the activity of coumarin anticoagulants; testosterone may enhance the activity of oral antidiabetics.
## GP responsibilities

1. Provide family with advice on the need for investigation of the child’s delayed puberty.
2. Confirm or decline request to share patient’s care within 10 working days, using the shared care request form.
3. Arrange administration of the second and subsequent injections.
4. Monitor the patient’s overall health and well being and observe patient for evidence of ADRs/abnormalities and raise with secondary care clinician if necessary.
5. Prescription of drug after initiation by secondary care.
6. For HH/PTF individuals, monitor FBC (to include haematocrit and haemoglobin) every 3 months for the first year and then annually thereafter along with LFTs & lipids annually.
7. Comply with terms of the Community Based Service and any national advice on testosterone.
8. Ensure advice is sought from the secondary care clinician if there is any significant change in the patient’s physical health status.
9. Agree long term therapy and predicted benefits in line with secondary care clinician’s original request.

## Community pharmacist responsibilities

1. Check patient is taking the medicine as prescribed
2. Check the patient is attending for monitoring as outlined above
3. Report any side effects to the GP

## Patient responsibilities

1. Do not miss any blood tests or other appointments without first consulting the GP or specialist.
2. Report any adverse effects or warning symptoms to the GP or specialist.

## Background:

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 HH and PTF. Testosterone replacement therapy is used to induce development of secondary sexual characteristics and promote linear growth, normal accrual of muscle mass and bone mineral density while avoiding premature epiphyseal plate closure. Testosterone replacement therapy is usually started from the age of 13-14 years and dose increased progressively over 24-36 months so adult maintenance dose is established. The maintenance dose of testosterone replacement is continued into adult life.

CDGP is the most common cause of delayed puberty (absence of signs of secondary sexual development i.e. testicular volume < 4 mls in a boy aged 14 years or more). They often 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 psychosocial wellbeing. As CDGP is considered a variant of normal growth, vast majority can be successfully managed by reassurance and observation. However, a short course of low dose testosterone treatment can be offered in order to enhance growth rate and expedite the features of puberty without affecting final height outcome in boys over the age of 14 years who are demonstrating features of delayed puberty and consequent distress. In this selected group who receive treatment, the intervention is well tolerated, highly effective and regarded as a standard therapeutic option.
It can be extremely difficult in early stages to differentiate CDGP from HH. In such a scenario, the recommendation is to provide short course testosterone treatment in the first instance and monitor closely. A second course of treatment may be necessary in some individuals before the situation becomes clearer and replacement therapy planned if the diagnosis of HH is considered. Increase in testicular size represents a subtle yet key factor pointing to a diagnosis of CDGP rather than HH. Hence, close monitoring of growth and pubertal status is paramount in boys who receive testosterone replacement treatment.

**Testosterone Preparations:**

British Society for paediatric endocrinology and diabetes (BSPED) recommend several licensed preparations of testosterone for use off-label in children, including the injectable, oral capsule and testosterone cream/gel. Other licensed testosterone preparations that are available (transdermal gel, patch and implant) are not recommended by BSPED for use in children.

**Injectable testosterone preparations:**

First choice of preparation recommended for children and adolescents

1) Long-acting testosterone ester (testosterone enantate (Alliance) 250mg/mL
2) Mixture of esters (Sustanon 250®) if enantate unavailable

**Dose regime and duration of therapy:**

1) CDGP – Testosterone 100 mg monthly IM for 4 doses only.
2) Hypogonadism due to HH or PTF: Testosterone 50 mg per month is used initially and escalated by 50 mg every 6 months to achieve a dose of 250 mg per month before changing to standard injectable adult dose of 250mg 3 weekly. This process may take 2½ to 3 years to be established.

**Side-effects:**

Local discomfort at injection site due to oily preparation can be rarely associated – injection site should be varied periodically to minimise this.

Others (very rare) – headache, nausea, gynaecomastia, weight gain

**Other preparations:**

Restandol® Testocaps (Organon) is an alternative preparation that is available if injection is not tolerated (side-effects, needle phobia). The dose is 40 mg once daily for 3 months in CDGP. In hypogonadism, starting at 40 mg once daily, dose is gradually titrated up every 6 months to a maximum dose of 80 mg tds after 2–3 years. Oral testosterone has a short half-life and must be taken with food for satisfactory absorption.

**Assessment of response to therapy:**

CDGP: Clinical review will be arranged 3-4 months after the 4th dose of testosterone injection. Assessment includes review of height, pubertal progress and to ensure young person and family are happy with the situation. Occasionally, a second course of injection may be necessary if there has been no progress. If there is any doubt about the diagnosis of CDGP, it is prudent to keep under clinical review until testicular volumes are 10 mL or more.

HH/PTF: Six monthly clinic review is essential to review growth and pubertal status and to titrate the testosterone dose depending on the response. Assessment of testicular volume is essential.
If any increase in testicular volume is noticed during therapy, the treatment has to be discontinued immediately and diagnosis reviewed. The testosterone treatment would need to be recommenced if the diagnosis of HH or PTF reconfirmed during phase when treatment was discontinued.

Whilst on testosterone replacement treatment, this group of boys will be reviewed in the transitional clinic for joint review with adult endocrinologist. Information will be provided on other non-injectable testosterone preparations that are available to choose once adult maintenance dose is established.

**Referral criteria:**

Children with delayed puberty should be referred to a hospital specialist with expertise in their assessment.

Children should not be placed on testosterone therapy before specialist evaluation has been completed.

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**Further advice and support - this information is not inclusive of all prescribing information**

| Summary of product characteristics via electronic Medicines Compendium (eMC) |
| British National Formulary via www.medicinescomplete.com |

Consultant Paediatric Endocrinologists
Secretary: 0116 258 7737
Safe haven fax: 0116 258 5567

Paediatric Endocrine specialist Nurse – Tel: 0116 258 5326
Paediatric Pharmacy Team – Tel 0116 254 1414 (ask for Pharmacy Satellite)

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Trent Medicines Information Centre, Victoria Building, Leicester Royal Infirmary, LE1 5WW
Tel: 0116 258 6491 Fax: 0116 258 5680
e-mail: medicines.info@uhl-tr.nhs.uk

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**Version control**

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