Triptorelin (Decapeptyl SR) in the treatment of Central Precocious Puberty

In December 2013, the LMSG approved the simple amber status of triptorelin for the treatment of central precocious puberty which means it can be prescribed and administered in primary care after specialist assessment and recommendation. A full shared care agreement is not required. Further information on simple amber medicines can be found in the Simple Amber Medicines – Principles for Prescribing document.

Information for Prescribers

Important points
- Central Precocious Puberty (CPP) is due to premature activation of the hypothalamo-pituitary axis, and consequently not only the pattern, but also the consonance of puberty in CPP is the same as that seen in normal puberty.
- CPP almost certainly represents a spectrum of disease from a normal variant to rapidly progressive disease.
- The estimated incidence is 1 in 5,000 to 10,000.

Central precocious puberty (CPP) is a form of premature sexual maturation, with the early appearance of secondary sexual characteristics –

In girls - Breast development before 8 years of age. Menarche before 9 years of age.
In boys - Genital development (including testicular enlargement) before 9 years of age.

There has been a secular trend downwards in the age of puberty, and it has now been suggested that the cut-off age of precocious puberty for girls should be reduced to 7 years (and 6 years in those of Afro-Caribbean origin).

Other features of precocious puberty are:
- Development of pubic and axillary hair.
- Tall stature, especially in relation to parental heights.
- Rapid growth rate.
- Advanced skeletal maturation (assessed using bone age).

Causes of CPP:
- Idiopathic: Sporadic, familial
- Organic: CNS tumours malformation, infection

Overall, 90% of affected patients are female. Idiopathic CPP occurs in only 30% of males, but in up to 80% of females.
There is overlap in the clinical and biochemical features of idiopathic and organic CPP. As a result it is currently recommended that all patients with CPP have MRI scanning of the brain (including pituitary and hypothalamus). Occult intra-cranial tumours are found in 4.8-13.3% of girls and 19.2% of boys with CPP.

**Problems arising from CPP**

- Social and psychological problems of tall stature, early development (and menarche).
- Loss of final height.

The aims of treatment are, therefore, to hold pubertal development in an emotionally immature child.

**Indications for therapy**

- True precocious puberty due to premature activation of the hypothalamic-pituitary-gonadal axis.
- Where puberty needs to be delayed in order to maximise growth potential e.g. Growth hormone deficient children following cranial irradiation, congenital adrenal hyperplasia.

**Gonadotrophin releasing-hormone (GnRH) analogues**

These are used in paediatric practice for the suppression of precocious puberty. There are several preparations currently available;

- Buserelin.
- Leuprorelin.
- Triptorelin.

**Injectable GnRH Agonists**

Triptorelin (Decapeptyl SR, Ipsen) is the only licensed 3 monthly GnRH agonist for the treatment of CPP in children. The dose is 11.25mg for all patients and the first dose is given by UHL. Repeat doses are required every 12 weeks. Rarely, the frequency may be reduced to every 10/11 weeks if the child advances in puberty on 12 weekly treatment.

**Mode of action of GnRH agonists**

All of these drugs are synthetic analogues of naturally occurring GnRH which possess greater potency than the natural hormone, binding to the GnRH receptor. As a result there is an initial period of stimulation, which can be blocked using the anti-androgen cyproterone acetate, given (usually) for the first six weeks of therapy at a dose of 70mg/m²/day.

Chronic administration results in an inhibition of gonadotrophin production and subsequent suppression of ovarian and testicular steroid production. These effects are reversible on discontinuation of therapy.
Assessment of response to therapy

Development of 2° sexual characteristics, uterine/ovarian size, growth rate & bone maturation should be monitored clinically, sonographically & radiologically.

The best single test is probably GnRH stimulation. Basal serum testosterone levels may be useful in boys, but conversely oestradiol appears not to be as useful in girls.

Side-effects – very rare -

- Local irritation: site with sc. or im. analogues (the injection site should be varied periodically), hot flushes, and mood swings.
- Hypersensitivity: rashes pruritus, asthma & rarely anaphylaxis.
- Others: headache, visual disturbance, dizziness, arthralgia/myalgia, hair loss, peripheral oedema, GI disturbances, weight gain, sleep disorders.

Duration of therapy

Once started, treatment is generally continued until an age when puberty can be allowed to recommence. This will vary with each child, but will tend to be at around 11-12 years of age.

Outcomes

- GnRH agonist treatment does not improve final height in girls beyond 8 years of age.
- Results are not as good in boys as girls.
- 75% of patients reach their genetic target height range.
- 40% reach their individual target height range.
- More than 90% of females have a final height > 150cm.

Complete reversibility of hypothalamo-pituitary gonadal axis has been demonstrated after discontinuation of therapy. Fertility & pregnancy outcome are unaffected in women (although an increase in polycystic ovarian syndrome (PCOS) has been described in some). Spermatogenesis is unaffected in men.

Referral criteria

- Children with precocious puberty should be referred to a hospital specialist with expertise in their assessment.
- Children should not be placed on the GnRH analogue therapy before specialist evaluation has been completed.

The consultant will recommend commencing triptorelin, and will provide the GP with a full report justifying GnRH analogue therapy.

Guidelines for shared care strategy

When initially commenced on a GnRH analogue, a child with precocious puberty will require more frequent hospital supervision to ensure and adequate response and will receive ongoing follow-up in the hospital environment while on this therapy.
GP responsibilities

- Providing family with advice on the need for investigation of the child’s precocious puberty.
- Prescribing the GnRH analogue when requested by specialist.
- Arranging that someone from the practice/community will be available to administer the second and subsequent injections.
- Reporting adverse effects of therapy to specialist or deputy.

Endocrine specialist responsibilities

- Arranging for the first injection to be given by the endocrine clinic specialist nurse in hospital.
- Reviewing 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.
- Advising GP as to continued justification for GnRH analogue therapy.
- Reviewing associated drug therapy.
- Auditing patient’s response to GnRH analogue therapy compared to nationally agreed criteria.
- To inform GP when treatment should be discontinued.

Contact for support and advice

Dr Savitha Shenoy – Consultant Paediatric Endocrinologist – Sec 0116 258 7737
Dr James Greening – Consultant Paediatric Endocrinologist – Sec 0116 258 7737
David Harris – Principal Pharmacist, Womens & Children’s Services – 0116 258 5761

Consult the SPC for full details of the drug (dosage, side effects, interactions etc).

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

Version controls log

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<td>01/06/2015</td>
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<td>1.2</td>
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<td>Addition that a shared care agreement is not required. Removal of GP responsibility to find out length of treatment as consultant responsibility.</td>
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