Degarelix depot (Firmagon) for advanced, hormone-dependent prostate cancer

September 2007

This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.
Degarelix depot (Firmagon) for advanced, hormone-dependent prostate cancer

**Target group**
- Men with locally advanced or metastatic hormone-dependent prostate cancer

**Background**
Testosterone is essential for the continuing growth and proliferation of prostate cancer cells, and hormonal strategies (androgen suppressing) are the mainstay of the management of advanced prostate cancer. Current hormonal options include gonadotrophin-releasing hormone (GnRH) analogues. However, although these therapies are effective in reducing testosterone, they stimulate testosterone production before shutting it down, which can lead to a tumour flare in susceptible patients, with the risk of spinal cord compression, ureteric obstruction and/or increased bone pain. To counter this risk an anti-androgen is usually administered for the first three weeks of GnRH therapy.

**Technology description**
Degarelix depot (Firmagon) is a GnRH receptor blocker that stops the release of luteinising hormone (LH) and follicle stimulating hormone (FSH) from the anterior pituitary gland rapidly reducing the production of testosterone by the testes. Degarelix depot does not induce a tumour flare, and is administered as a depot subcutaneous injection every 28 days.

**Innovation and/or advantages**
Degarelix depot belongs to a new class of drug - GnRH receptor blockers. It does not induce tumour flare and will reduce the need for additional anti-androgen therapy.

**Developer**
Ferring Pharmaceuticals

**Place of use**
- Home care e.g. home dialysis
- Secondary care e.g. general, non-specialist hospital
- Community or residential care e.g. district nurses, physio
- Tertiary care e.g. highly specialist services or hospital
- General public e.g. over the counter
- Primary care e.g. used by GPs or practice nurses
- Emergency care e.g. paramedic services, trauma care
- Other:

**Availability, launch or marketing dates, and licensing plans:**
Degarelix depot is in phase III clinical trials.

**NHS or Government priority area:**
- Cancer
- Diabetes
- Older people
- Women’s health
- Cardiovascular disease
- Long term neurological conditions
- Public health
- None identified
- Children
- Mental health
- Renal disease
- Other:

This topic is relevant to the NHS Cancer Plan.
Relevant guidance

Clinical need and burden of disease
Prostate cancer is the commonest cancer diagnosed in men in the UK, with 28,867 new cases registered in 2003 in England and Wales⁴. More than 60% of cases are diagnosed in men over the age of 70. There were 9,013 deaths from prostate cancer in England and Wales in 2005⁴. The 5-year survival rate for men diagnosed in England in 2000–01 was 71%.

The majority of newly diagnosed prostate cancer is initially hormone dependent with advanced cancer generally responding to hormone manipulation for around 12 to 18 months.

Existing comparators and treatments
Treatment options for locally advanced disease include radiotherapy, hormonal therapy, high intensity focused ultrasound, and cryotherapy. Hormonal therapy options include:
- GnRH analogues e.g. buserelin, goserelin, leuprorelin or triptorelin.
- Anti-androgens e.g. cyproterone acetate, flutamide or bicalutamide, are used in patients at risk of tumour flare during the initiation of GnRH analogue therapy. Therapy to reduce tumour flare is initiated 3 days prior to the GnRH analogue and continued for 3 weeks.
- Bilateral orchidectomy

Efficacy and safety

<table>
<thead>
<tr>
<th>Trial name or code</th>
<th>Phase II and extension</th>
<th>Phase II</th>
<th>Phase II</th>
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<tbody>
<tr>
<td>Sponsor</td>
<td>Ferring</td>
<td>Ferring</td>
<td>Ferring</td>
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<tr>
<td>Status</td>
<td>Conference abstracts ⁵,⁶,⁷</td>
<td>Conference abstract ⁸</td>
<td>Conference abstract ⁹</td>
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<tr>
<td>Location</td>
<td>Europe, South Africa</td>
<td>Europe</td>
<td>UK</td>
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<tr>
<td>Design</td>
<td>Randomised phase, then extension using the same maintenance dose.</td>
<td>Dose escalation</td>
<td>Randomised</td>
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<td>Participants in trial</td>
<td>n=187; age 52-93; prostate cancer with prostate-specific antigen (PSA) ≥2ng/ml; 19% had metastatic; 32% locally advanced; and 22% localised cancer. Randomised to degarelix: 200mg or 240mg initiation dose; and 80, 120 or 160mg maintenance doses every 28 days.</td>
<td>n=172; age 48-89; histologically confirmed prostate cancer, PSA ≥2ng/ml. Single doses of 120mg, 240mg and 320mg degarelix at different concentrations.</td>
<td>n=129 age 55-89; early and late stage prostate cancer with PSA ≥20ng/ml. 33% had metastatic; 46% locally advanced; and 17% localised cancer. Randomised to degarelix: A: 160mg induction &amp; 40mg maintenance every 28 days; B: 80mg &amp; 40mg; or C: 80mg &amp; 20mg.</td>
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</table>

¹ Docetaxel for hormone-refractory prostate cancer. NICE Technology Appraisal. 2006.
<table>
<thead>
<tr>
<th>Follow-up</th>
<th>1 year (phase II) 2 years (extension study)</th>
<th>28 days</th>
<th>6 months</th>
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<tr>
<td>Primary outcome</td>
<td>Testosterone and PSA levels.</td>
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<tr>
<td>Key results</td>
<td>Phase II: Initiation dose 200mg: 88% had testosterone ≤0.5ng/ml at day 2; and 86% by day 28. Initiation dose 240mg: 92% had testosterone ≤0.5ng/ml at day 2; and 95% by day 28. Maintenance dose 160mg: 100% had testosterone ≤0.5ng/ml at each monthly visit, compared to 96% of those on 120mg and 92% on 80mg. Extension study: Maintenance dose 160mg: 95% had testosterone consistently ≤0.5ng/ml compared to 86% of those on 120mg.</td>
<td>N=169 evaluated up to day 28. Higher doses but at lower concentration were better at suppression of testosterone. 96% of men given 240mg (at 40mg/ml) achieved testosterone ≤0.5ng/ml.</td>
<td>N=102 evaluated. At 6 months sustained testosterone reduction ≤0.5ng/ml found in 87.5% of group A; 72.2% of group B, and 58.8% of group C. In group A testosterone was ≤0.5ng/ml in 97.5% within 3 days, and in 100% by 28 days.</td>
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<tr>
<td>Major adverse effects</td>
<td>No evidence of testosterone surge. 12 patients withdrew (phase II) due to adverse effects most related to androgen depletion. 23 patients withdrew (extension) due to cardiovascular or disease progression.</td>
<td>The most frequently reported adverse effects were related to androgen depletion.</td>
<td>6 patients withdrew – most due to the effects of androgen depletion. 18 withdrawn from trial for reasons other than lack of efficacy.</td>
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<tr>
<th>Trial name or code</th>
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<th>Phase III 3-month formulation</th>
<th>Phase III NCT00295750 (vs. luprolide)</th>
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<td>Location</td>
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<td>Design</td>
<td>Randomised</td>
<td>Randomised, open-label</td>
<td>Randomised, open-label</td>
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<td>Participants in trial</td>
<td>n=127, age 47-93; prostate cancer with PSA ≥2ng/ml. Degarelix initial dose 200mg then maintenance of 60mg or 80mg every 28 days.</td>
<td>Planned n=100; 2 different doses of a 3-month formulation of degarelix.</td>
<td>Planned n=675. Randomised to degarelix 160mg and 80mg every 28 days, or luprolide depot 7.5mg.</td>
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<tr>
<td>Follow-up</td>
<td>1 year</td>
<td>1 year</td>
<td>1 year</td>
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<tr>
<td>Primary outcome</td>
<td>Testosterone and PSA levels.</td>
<td>Testosterone and PSA levels.</td>
<td>Non-inferiority in testosterone and PSA levels.</td>
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<tr>
<td>Key results</td>
<td>After initial dose 88% had testosterone ≤0.5ng/ml at day 28. Of these 98% on 80mg maintenance dose and 93%</td>
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on 60mg had testosterone levels consistently ≤0.5ng/ml to 1 year.

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<th>Expected reporting date</th>
<th>Study start May 2007</th>
<th>Study start February 2006. Last patients visit expected at the end of 2007</th>
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<td>Major adverse effects</td>
<td>No evidence of testosterone surge. 6 patients withdrew – only 1 related to treatment (injection site urticaria).</td>
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**Estimated cost and cost impact**

The cost of degarelix depot has yet to be determined.

Goserelin costs around £1,100 for a year’s treatment. Leuprorelin costs around £1,500 per year. Anti-flare with cyproterone acetate for 3 weeks costs up to £90 – depending on dose and duration.

**Potential or intended impact – speculative**

- **Patients**
  - ☑ Reduced morbidity
  - ☑ Improved quality of life for patients and/or carers
  - ☑ Quicker, earlier or more accurate diagnosis or identification of disease
  - ☑ Reduced mortality or increased survival
  - ☑ Non identified
  - ☐ Other:

- **Services**
  - ☐ Increased use
  - ☑ Service reorganisation required
  - ☑ Staff or training required
  - ☐ Decreased use
  - ☑ Other:
  - ☑ Non identified

- **Costs**
  - ☐ Increased unit cost compared to alternative
  - ☑ Increased costs: more patients coming for treatment
  - ☑ Increased costs: capital investment needed
  - ☑ Savings: reduced need for anti-androgen, anti-flare medication
  - ☑ Other: Uncertain cost impact

**References**


