NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Degarelix for treating advanced hormone-dependent prostate cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of degarelix within its licensed indication for the treatment of advanced hormone-dependent prostate cancer.

Background

Prostate cancer is a disease in which tumours develop in the prostate, a gland in the male reproductive system. Its cause is thought to involve both environmental and genetic factors. The incidence of prostate cancer increases with age and is higher in men of African-Caribbean family origin. In England and Wales, there were over 36,000 people newly diagnosed with prostate cancer in 2009 and over 9600 deaths from prostate cancer in 2010.

NICE clinical guideline 58 'Prostate cancer: diagnosis and treatment' recommends that people with localised disease should be offered active surveillance, prostatectomy (surgical removal of the prostate) or high-dose radical radiotherapy. Long-term disease-free intervals are commonly associated with surgical or radiotherapeutic treatment in more than 60% of people with localised disease but this is uncommon in people with advanced prostate cancer. Advanced prostate cancer is defined as locally advanced or metastatic disease (that is, where the cancer has spread beyond the prostatic capsule). Around 55–65% of people with prostate cancer develop metastatic disease.

NICE clinical guideline 58 recommends hormonal therapy for people with locally advanced prostate cancer who are receiving radical radiotherapy. Treatment with gonadotrophin-releasing hormone (GnRH) agonist therapy is recommended before and during radical radiotherapy. Hormonal therapy is additionally recommended after radical radiotherapy for those with a Gleason score of at least 8 (which indicates a poorer prognosis).

NICE clinical guideline 58 also recommends hormonal therapy for people with prostate cancer who experience a biochemical relapse after radical (prostatectomy or radiotherapy) treatment if they have symptomatic local disease progression, metastases or a prostate-specific antigen doubling time of less than 3 months. Standard hormonal treatments for metastatic disease are use of a GnRH agonist, such as goserelin, leuprorelin or triptorelin, or bilateral orchidectomy (surgical removal of the testes). Bicalutamide monotherapy is a treatment option for people with metastatic prostate cancer who are willing to accept the adverse impact on overall survival and

gynaecomastia (enlargement of breast tissue) in the hope of retaining sexual function.

During the first weeks of GnRH agonist therapy, an initial and temporary rise in serum testosterone (flare-up) can cause unwanted effects, which may in clinical practice be managed using anti-androgens. The clinical impact of the flare-up is unknown, except in patients with impending spinal cord compression for whom other strategies for immediately ablating testosterone levels, such as bilateral orchidectomy, should be considered.

The technology

Degarelix (Firmagon, Ferring Pharmaceuticals) is a selective gonadotrophin releasing hormone (GnRH) antagonist that reduces the release of gonadotrophins by the pituitary, which in turn reduces the secretion of testosterone by the testes. Because they do not produce a rise in hormone levels at the start of treatment, GnRH antagonists do not initially induce testosterone surge or tumour stimulation, or have the potential for symptomatic flare. Degarelix is administered as a subcutaneous injection.

Degarelix has a UK marketing authorisation for the "treatment of adult male patients with advanced hormone-dependent prostate cancer" (that is, where the cancer has spread beyond the prostatic capsule).

Intervention	Degarelix
Population	Adults with advanced hormone-dependent prostate cancer (locally advanced or metastatic, including biochemical relapse) in whom orchidectomy is not preferred
Comparators	• Gonadotrophin-releasing hormone agonists in combination with short-term anti-androgen treatment including: – Goserelin – Leuprorelin – Triptorelin • Bicalutamide

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • testosterone response • prostate-specific antigen (PSA) response • time to PSA progression • PSA progression-free survival • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If evidence allows, the following subgroups will be considered: high-risk patients with PSA >20 ng/mL; patients with spinal metastases with impending or actual spinal cord compression; patients with high tumour volume with impending or actual urinary outflow obstruction: patients with bony metastases associated with intractable pain; patients for whom standard anti-androgen treatment is contraindicated; patients at risk of evolving cardiovascular comorbidity. Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Guidelines: Cancer Service Guidance Urological Cancer, September 2002, Improving outcomes in urogenital cancers'. Anticipated review date TBC. Clinical Guideline No. 58, February 2008, 'Prostate cancer: diagnosis and treatment'. Currently under review (publication expected January 2014). Related Pathway: NICE Pathway, 'Prostate cancer' [http://pathways.nice.org.uk/pathways/prostate-cancer; accessed 15 August 2012].