Health Technology Briefing
September 2023

Degarelix acetate prior to or with radiotherapy for prostate cancer

Company/Developer	Ferring Pharmaceuticals Ltd

☐New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 35929	NICE TSID: Not Available	UKPS ID: 661153

Licensing and Market Availability Plans

Currently in phase 3 clinical trials.

Summary

Degarelix acetate is approved for the treatment of advanced hormone dependant prostate cancer and treatment of high risk localised or locally advanced prostate cancer, in combination with or prior to radiotherapy. Prostate cancer is a cancer of the prostate gland (a small organ in a man's pelvis) and is the most common cancer in men in the UK. The symptoms may vary depending on the stage of cancer but can include pain, tiredness, and problems emptying the bladder and the bowels. Prostate cancer growth and spread depends on the hormone testosterone. Locally advanced prostate cancer is cancer that has started to break out of the prostate, or has spread to the area just outside the prostate.

Testosterone can make prostate cancer cells grow. Degarelix acetate reduces the amount of testosterone in the body by blocking the effects of a natural hormone called gonadotrophin-releasing hormone (GnRH). GnRH is the first step in a pathway responsible for testosterone production. By blocking GnRH, degarelix acetate slows down the growth of the cancer cells. When injected under the skin, degarelix acetate forms a gel under the skin that releases the active substance slowly over a month. The extended licence for, degarelix acetate, with or without radiotherapy, can give patients with high-risk localised or locally advanced prostate cancer potential for a more effective treatment option.

This briefing reflects the evidence available at the time of writing 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 or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.
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Proposed Indication

For treatment of patients with very high risk localised or locally advanced prostate cancer.[1]

Technology

Description

Degarelix acetate (Firmagon) is a selective gonadotrophin releasing-hormone (GnRH) antagonist that competitively and reversibly binds to the pituitary GnRH receptors, thereby rapidly reducing the release of the gonadotrophins, luteinizing hormone (LH) and follicle stimulating hormone (FSH), and thereby reducing the secretion of testosterone by the testes. Prostatic carcinoma is known to be androgen sensitive and responds to treatment that removes the source of androgen. Unlike GnRH agonists, GnRH antagonists do not induce a LH surge with subsequent testosterone surge/tumour stimulation and potential symptomatic flare after the initiation of treatment.[2]

Degarelix acetate is/was in phase 3 clinical development (NCT02799706, NCT00833248, NCT00884273, NCT00831233) for the treatment of patients with very high risk or locally advanced prostate cancer.[1,3-5] Degarelix will be given at the dose of 240mg via two subcutaneous injections of 120mg at a concentration of 40mg/mL on day 1, followed by 80mg given as one subcutaneous injection at a concentration of 20mg/mL every 28 days.[1]

Key Innovation

Based on its mechanism of action, the European Medicines Agency (EMA) and MHRA considered that degarelix acetate can be expected to be effective for high-risk localised or locally advanced prostate cancer in combination prior to or with radiotherapy. It is known that treatment with degarelix does not trigger the temporary sharp rise in testosterone levels seen with 'GnRH agonists' (other medicines for prostate cancer that mimic the action of GnRH).[a]
This means that patients do not need to take other medicines to block testosterone at the start of treatment.[2] The extended licence for degarelix acetate can give patients with high-risk localised or locally advanced prostate cancer potential for a more effective treatment option (awarded in 2022).[6]

Regulatory & Development Status

Degarelix acetate currently has Marketing Authorisation in the EU/UK for the following indications:[7]

- For treatment of adult male patients with advanced hormone-dependent prostate cancer.
- For treatment of high-risk localised and locally advanced hormone dependent prostate cancer in combination with radiotherapy.
- As neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced hormone dependent prostate cancer.

Degarelix acetate is currently in phase 2 and 3 clinical trials for the treatment of various other lines of prostate cancer and breast cancer.[8]

Patient Group

[a] Information provided by Ferring Pharmaceuticals.

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Disease Area and Clinical Need

Prostate cancer is the most common cancer in men in the UK and is most common in older men.[9] It affects the prostate, a small gland in the pelvis found only in men which is located between the penis and the bladder and surrounds the urethra. The main function of the prostate is to help in the production of semen.[10] Localised prostate cancer is cancer that is only inside the prostate gland. It has not spread to other parts of the body and locally advanced prostate cancer means the cancer has broken through the capsule (covering) of the prostate gland. It has spread to nearby tissues, such as the rectum.[9] High risk means the tumours extend outside the prostate. There is also a subset of very aggressive tumours called "very high risk" in which the tumour has extended into the seminal vesicles or the rectum or bladder, or there are multiple biopsy samples with high grade cancer.[11] Prostate cancer is more common in black Caribbean and black African men than in white men and is less common in Asian men.[9] It's not known exactly what causes prostate cancer, although a number of things can increase your risk of developing the condition. These include; age, ethnicity, family history, obesity and diet.[12] Prostate cancer does not usually cause any symptoms until the cancer has grown large enough to put pressure on the urethra.[10] Prostate cancer is a significant cause of morbidity and mortality in men, especially in those over the age of 75 years and impacts on their daily lives, particularly physical and emotional health, relationships and social life.[13]

Prostate cancer accounts for 27% of all new cancer cases in males in the UK (2016-2018 data).[14] In England, in 2017 there were 41,201 registrations of newly diagnosed cases of malignant neoplasm of prostate (ICD-10 code C61).[15] According to Hospital Episode Statistics (HES) data, in 2021-22 there were 73,256 admissions with a primary diagnosis of neoplasm of the prostate (ICD-10 code C61), resulting in 77,547 finished consultant episodes (FCE), 71,095 bed days and 54,896 day cases.[7] In England and Wales in 2021, there were 10,367 deaths where malignant neoplasm of prostate (ICD-10 code C61) was recorded as the underlying cause.[16]

Recommended Treatment Options

According to National Institute for Health and Care Excellence (NICE) guidance, current treatment options for locally advanced prostate cancer include:[17]

- Active surveillance
- Radical prostatectomy
- Radical radiotherapy

Clinical Trial Information

Trial	**PEGASUS,** NCT02799706, Phase IIIb Randomized Trial Comparing Irradiation Plus Long Term Adjuvant Androgen Deprivation With GnRH Antagonist Versus GnRH Agonist Plus Flare Protection in Patients With Very High Risk Localized or Locally Advanced Prostate Cancer. A Joint Study of the EORTC ROG and GUCG. **Phase III** - Active, not recruiting **Locations:** UK and 7 EU countries **Primary completion date:** June 2024
Trial Design	Randomised, parallel assignment, open label.
Population	N=885 (planned), aged 18-80 years, males with histologically confirmed diagnosis of prostate adenocarcinoma.

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Intervention(s)	Degarelix acetate (SC) Radiotherapy
Comparator(s)	Matched placebo Radiotherapy
Outcome(s)	Primary outcome measures: • Progression free survival [Time frame: through study completion, an average of 1 year] See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	NCT00833248, EudraCT 2008-005232-33, A Randomised, Parallel Arm, Open-label Trial Comparing Degarelix With Goserelin Plus Anti-androgen Flare Protection (Bicalutamide), in Terms of Prostate Size Reduction in Prostate Cancer Patients of Intermediate-to-high Risk, Who Require Neoadjuvant Hormone Therapy Prior to Radiotherapy (Curative Intent). **Phase III:** Completed **Locations:** UK, US and 5 EU countries **Actual completion date:** September 2011
Trial Design	Randomised, parallel assignment, open label.
Population	N=246 (actual), aged 18+, males with confirmed prostate cancer.
Intervention(s)	Degarelix (SC 240mg/80mg)
Comparator(s)	Goserelin (3.6mg) + bicalutamide (50mg) (SC)
Outcome(s)	Primary outcome measures: • Change from baseline in prostate size based on trans rectal ultra sound (TRUS) at week 12 (full analysis set) [Time frame: after treatment of 12 weeks compared to baseline] • Change from baseline in prostate size based on TRUS) at week 12 (Per protocol analysis set) [Time frame: after treatment of 12 weeks compared to baseline] See trial record for full list of outcomes.
Results (efficacy)	The total prostate volume decreased significantly from baseline to week 12 in both treatment groups, reaching -36.0 ± 14.5% in degarelix-treated patients and -35.3 ± 16.7% in goserelin-treated patients (adjusted difference: -0.3%; 95% confidence interval: -4.74; 4.14%). At the end of the therapy, more degarelix- than goserelin-treated patients reported International Prostate Symptom Score decreases of ≥3 points (37% versus 27%, P = 0.21). In addition, in patients with a baseline International Prostate Symptom Score of ≥13, the magnitude of the decrease was larger in degarelix- (n = 53) versus goserelin-treated patients (n = 17) (6.04 versus 3.41, P = 0.06).[18]

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Results (safety)	Treatment-emergent adverse events that were considered possibly/probably related to the drug (i.e., adverse drug reactions) were reported by 78 and 73% of patients in the degarelix and goserelin groups, respectively. Most of the treatment-emergent adverse drug reactions were hot flushes (60% degarelix, 63% goserelin). Other commonly reported reactions were injection site reactions (predominantly pain 33%, erythema 25%, pruritus 7% and swelling 6%), which were reported by degarelix-treated patients only, erectile dysfunction (8% degarelix, 9% goserelin), asthenia (7 and 9%), fatigue (6 and 9%) and decreased libido (7 and 6%).[18]

Clinical Trial Information	
Trial	NCT00884273, EudraCT 2008-008604-40, A Randomised, Parallel-arm, Open-label Trial Comparing Degarelix With Goserelin Plus Anti-androgen Flare Protection (Bicalutamide), in Terms of Volume Reduction of the Prostate in Patients With Prostate Cancer Being Candidates for Medical Castration. **Phase III:** Completed **Locations:** 6 EU countries, Norway and Turkey **Actual completion date:** March 2011
Trial Design	Randomised, parallel assignment, open label.
Population	N=182 (actual), aged 18+, males with confirmed prostate cancer.
Intervention(s)	Degarelix (SC 240mg/80mg)
Comparator(s)	Goserelin (3.6mg) + bicalutamide (50mg) (SC)
Outcome(s)	Primary outcome measures: • Change from baseline in prostate size based on TRUS at week 12 (Full analysis set) [Time frame: after treatment of 12 weeks compared to baseline] • Change from baseline in prostate size based on TRUS at week 12 (Per protocol analysis set) [Time frame: after treatment of 12 weeks compared to baseline] See trial record for full list of outcomes.
Results (efficacy)	While the short-term efficacy of degarelix and goserelin + bicalutamide was the same in terms of total prostate volume (TPV) reduction, degarelix showed superiority in lower urinary tract symptoms (LUTS) relief in symptomatic patients, which could highlight the different actions of these drugs on extrapituitary gonadotrophin-releasing hormone (GnRH) receptors in the bladder and/or the prostate.[19]
Results (safety)	Both treatments were safe and well tolerated.[19]

Clinical Trial Information

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Trial	NCT00831233, EudraCT 2008-004338-26, A Randomised, Parallel-arm, Open-label Trial Comparing Degarelix With Goserelin Plus Anti-androgen Flare Protection (Bicalutamide), in Terms of Reduction in International Prostate Symptom Score (IPSS), in Patients With Lower Urinary Tract Symptoms (LUTS) Secondary to Locally Advanced Prostate Cancer. **Phase III:** Terminated (Poor recruitment due to rare targeted population) **Locations:** UK and 2 EU countries **Actual study completion date:** June 2010
Trial Design	Randomised, parallel assignment, open label.
Population	N=42 (actual). Aged 18+, males with confirmed prostate cancer diagnosis.
Intervention(s)	Degarelix (SC 240mg/80mg)
Comparator(s)	Goserelin (SC 3.6 mg) + bicalutamide (oral 50 mg)
Outcome(s)	Primary outcome measures: • Change from baseline in total international prostate symptom score (IPSS) at week 12 [Time frame: after treatment of 12 weeks compared to baseline] See trial record for full list of outcomes
Results (efficacy)	This study was stopped early due to recruitment difficulties. Forty patients received treatment (degarelix n = 27; G+B n = 13); most had locally advanced disease and were highly symptomatic. Degarelix was non-inferior to goserelin plus bicalutamide in reducing IPSS at week 12 in the full analysis set (p = 0.20); the significantly larger IPSS reduction in the per-protocol analysis (p = 0.04) was suggestive of superior reductions with degarelix. Significantly more degarelix patients had improved quality of life (IPSS question) at week 12 (85 vs. 46%; p = 0.01). Mean prostate size reductions at week 12 were 42 versus 25% for patients receiving degarelix versus G+B, respectively (p = 0.04; post hoc analysis).[20]
Results (safety)	Most adverse events were mild/moderate; more degarelix patients experienced injection site reactions whereas more goserelin plus bicalutamide patients had urinary tract infections/cystitis.[20]

Estimated Cost

Degarelix acetate is already licensed for the treatment of prostate cancer. An 80mg powder and solvent for solution for injection vial costs £129.37 and an 120mg powder and solvent for solution costs £260.[21]

Relevant Guidance

NICE Guidance

- NICE clinical guideline. Prostate cancer: diagnosis and management (NG131). December 2021.
- NICE quality standard. Prostate cancer (QS91). December 2021.
- NICE Interventional procedures guidance. Focal therapy using high-intensity focused ultrasound for localised prostate cancer (IPG756). April 2023.

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NHS England (Policy/Commissioning) Guidance
• NHS England. 2013/14 NHS Standard Contract for Cancer: Specialised Kidney, Bladder and Prostate Cancer Services (Adult). B14/S/a. • NHS England. Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) in the treatment of Prostate Cancer. 16031/P. July 2016. • NHS England. Clinical Commissioning Policy: Proton Beam Therapy for Cancer of the Prostate. 16020/P. July 2016
Other Guidance
• European Association of Urology. Guidelines on Prostate Cancer. 2023.[22] • ESMO Guidelines Committee. Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2020.[23] • Public Health England. Prostate Cancer Risk Management Programme. March 2016.[24]

Additional Information

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