POSITION STATEMENT

Degarelix for treatment of adult male patients with advanced hormone-dependent prostate cancer without spinal metastases

RECOMMENDATION:

Degarelix should be recommended/initiated by specialist services– **AMBER0** recommendation.

Degarelix is recommended as an alternative to lutenising hormone releasing hormone agonists (LHRH) for treatment of adult male patients with advanced hormone-dependent prostate cancer **without** spinal metastases **ONLY** in the following circumstances:

- where LHRH analogues or concomitant anti-androgens are contra-indicated.
- in patients on androgen deprivation therapy who have a significant cardiac history/severe cardiac disease.
- very significant, symptomatic metastatic disease, and locally advanced disease to shrink the metastases.
- impending bladder outlet obstruction due to prostate cancer.

SWITCHING PATIENTS FROM DEGARELIX TO LHRH AGONISTS

For patients using Degarelix:

- in line with NICE TA 404 or;
- using degarelix in line with the recommendations above.

Patients can be switched to an LHRH agonist when their PSA levels have dropped to an undetectable level or nadir level is achieved. This will vary from patient to patient but on average occurs at 3 to 6 months following degarelix initiation. There will a limited number of patients who must remain on degarelix long term, and this should be clearly defined by specialists on discharge.

Prescribers should consider acquisition cost, patient preference and frequency of administration when selecting an LHRH agonist (see point 4 below for details of costs and regimens).

RATIONALE FOR RECOMMENDATIONS

Prescribing data indicates existing prescribing of degarelix for adult male patients with advanced hormone-dependent prostate cancer **without** spinal metastases, this recommendation is not anticipated to have a significant financial impact. Switching the majority of patients to LHRH agonist after 3-6 months is expected to be cost saving to the Lancashire and South Cumbria ICB.

1. BACKGROUND

There is no cure for prostate cancer if the disease has spread outside of the prostate gland to lymph nodes or to the bones. In such a situation, hormonal therapy that lowers levels of the male sex hormone testosterone can slow down cancer growth. Testosterone levels are regulated by complicated mechanisms that involve a hormone known as gonadotropin-releasing hormone (GnRH), which is present in men at different levels at different times of the day. It is understood that giving men with prostate cancer high levels of medications that increase GnRH levels first raises testosterone levels, and then drops them to very low levels. These medications are commonly used to treat men with prostate cancer that has spread outside the prostate. Degarelix is a drug known as a GnRH antagonist, which blocks receptors in the brain and thereby lowers testosterone levels immediately. [1]

2. CLINICAL EVIDENCE

NICE

NICE TA 404 states:

> Degarelix is recommended as an option for treating advanced hormone-dependent prostate cancer **in people with spinal metastases**, only if the commissioner can achieve at least the same discounted drug cost as that available to the NHS in June 2016 (*bold emphasis not in TA*) [2]

Background to NICE Appraisal

The National Institute for Health and Care Excellence (NICE) published a review of the evidence for degarelix (TA 404) derived from the company's evidence submission. They concluded that the GnRH antagonist degarelix was non-inferior to standard androgen suppression therapy regarding the reduction of testosterone levels, but achieved a more rapid suppression of the disease marker Prostate Specific Antigen (PSA). Degarelix also decreased the incidence of testosterone flare that is typically associated with GnRH agonists. This evaluation on behalf of NICE suggested that degarelix was not cost-effective for the subgroup with metastatic disease, but could be cost-effective for the subgroup with spinal metastases. However, it should be considered that the recommendation for degarelix in patients with impending spinal cord compression is based on the results of small (post hoc defined) subgroup analyses and on the assumption that rapid androgen suppression with prevention of testosterone flare might be clinically useful. Most participants included in randomized controlled trials had a nonadvanced disease stage, and the studies were not predefined to evaluate degarelix for this purpose. [1] [2]

SMC

The Scottish Medicines Consortium (SMC) accepted degarelix for use within NHS Scotland:

> for the treatment of adult male patients with advanced hormone-dependent prostate cancer. [3]

Background to SMC advice

This was based on one study that included patients with all stages of prostate cancer. Degarelix was shown to be non-inferior to a luteinising hormone releasing hormone (LHRH) agonist in suppressing testosterone levels over a one-year treatment period without an initial testosterone flare. [3]

COCHRANE REVIEW

The authors of the 2021 review *Degarelix for treating advanced hormone-sensitive prostate cancer* [1] concluded the following:

- it is unclear if degarelix has any effect on overall survival, cancer specific survival, or clinical progression because we did not identify data for these outcomes. Degarelix

likely results in no clinically meaningful difference in quality of life, and may result in similar serious adverse events compared to standard androgen suppression therapy.
- Injection site pain is likely increased with the use of degarelix.
- The effects of degarelix on cardiovascular events in a general population in clinical routine and on biochemical progression are very uncertain.
- While degarelix likely increases the total number of non-serious adverse events slightly, there were similar discontinuations due to adverse events. Degarelix probably reduces the rate of fatal adverse events, as it reduced mortality during study conduction slightly.
- Degarelix may reduce back pain slightly; likely reduces anaemia and urinary tract infections; but also likely increases hepatic enzyme increase compared to standard androgen suppression therapy.
- Subgroup analyses for different maintenance doses showed no difference between groups for serious adverse events, quality of life, and injection site pain.
- It remains unclear if different standard androgen suppression therapies or different stages of advanced hormone-sensitive prostate cancer (non-metastatic versus metastatic disease) affect these findings.

3. CURRENT USE OF DEGARELIX BY SPECIALISTS IN LANCASHIRE AND SOUTH CUMBRIA OUTSIDE OF NICE TA404 RECOMMENDATIONS

Clinicians from specialist urology departments have been consulted to establish how degarelix is used within their department.

- East Lancashire Hospitals Trust use degarelix in advanced hormone dependent prostate cancer where LHRH analogues or concomitant anti-androgens are contra-indicated.
- In Morecambe Bay specialists use degarelix in patients requiring androgen deprivation therapy who have a significant cardiac history, and also in patients with very significant, symptomatic metastatic disease, and locally advanced disease to shrink the metastases.
- Blackpool Teaching hospitals use degarelix If there are spinal metastases or impending bladder outlet obstruction due to prostate cancer (small numbers). Also degarelix is used if someone has severe cardiac disease (very occasionally).

4. CURRENT COSTS OF SUPPLYING DEGARELIX AND COST OF SUPPLYING LHRH ANALOGUES AFTER STABILISATION OF PATIENTS

Degarelix is supplied as an initial 240 mg dose followed by 80 mg as a subcutaneous monthly injection. The cost per patient per year is approximately £1,700 in the first year and £1,600 thereafter. Degarelix has an Amber0 RAG status in Lancashire and South Cumbria for advanced hormone-dependent prostate cancer with spinal metastases. According to ePACT data for the year to July 2022, the annual total spend for degarelix on FP10 prescription in Lancashire and South Cumbria was approximately £121,000. Please note, TA404 mandates that degarelix is supported only if a confidential discounted patient access scheme is applied.

Once patients have been stabilised on degarelix, local hospital trusts have suggested that it is possible to switch patients to LHRH agonists to improve treatment compliance and reduce costs. The table below contains examples of LHRH agonist regimens and costs which reduce frequency of administration and cost.

Drug	**Dose Regimen**	**Cost per year (£)**
Goserelin 10.8mg implant	One implant every 12 weeks	1018
Leuprorelin acetate 11.25mg injection	One injection every three months.	978

Triptorelin 22.5 mg injection (Decapeptyl® SR)	One injection every six months.	897

5. REFERENCES

[1] F Zengerling et al, "Degarelix for treating advanced hormone-sensitive prostate cancer," *Cochrane Database of Systematic Reviews,* p. CD012548. , 2021.

[2] National Institute for Health and Care Excellence, "Degarelix for treating advanced hormone-dependent prostate cancer," August 2016. [Online]. Available: https://www.nice.org.uk/guidance/ta404. [Accessed August 2022].

[3] Scottish Medicines Consortium, "Degarelix 120mg and 80mg powder and solvent for solution for injection (Firmagon)," December 2010. [Online]. Available: https://www.scottishmedicines.org.uk/media/1544/degarelix_firmagon_resubmission_final_december_2010doc_for_website.pdf. [Accessed August 2022].