Appendix G - professional organisation statement template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Degarelix for treating advanced hormone-dependent prostate cancer

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Dr Heather Payne

Name of your organisation: British Uro oncology Group (BUG)

Are you (tick all that apply):

- √ a specialist in the treatment of people with the condition for which NICE is considering this technology?
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc)?
- other? (please specify)

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

Androgen deprivation is the mainstay of treatment for advanced prostate cancer. The reduction in testosterone by surgical or medical means significantly slows the progression of the disease and also treats cancer related symptoms such as pain from bone metastases. Advanced prostate cancer is currently treated with first line LHRH agonists. After a period of time some cells develop resistance to this therapy and other drugs such as additional hormone manipulations or chemotherapy are added in a sequential fashion to the LHRH agonist which continues to be prescribed in addition to these other therapies.

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

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In contrast to LHRH agonists, GnRH antagonists bind immediately and competitively to LHRH receptors in the pituitary gland. The effect is a rapid decrease in LH, FSH and testosterone levels without any testosterone flare. In Phase III clinical trial data, degarelix demonstrates reduced testosterone concentrations to below castrate levels in 3 days (90% decrease in median testosterone compared with leuprolide group experiencing a 65% increase in median testosterone levels; p<0.001) This gives immediate benefit to men with advanced disease and faster symptom control. It also avoids the need to prescribe an antiandrogen to suppress the testosterone flare associated with LHRHagonists.

Degarelix shows long term suppression of testosterone for up to 364 days. 97.2% of patients on degarelix maintained medical castrate levels (<50 ng/dl from day 28 to Day 364 (95% /CIS) compared to 96.4% with leuprolide. PSA levels were lowered by 64% after 2 weeks, 85% after 1 month and 95% after 3 months and remained suppressed throughout the 1-year treatment. (Klotz L, Boccon-Gibod L, Shore ND *et al*. The efficacy and safety of degarelix: a 12-month, comparative, randomized, open-label, parallel-group phase III study in patients with prostate cancer. *BJU Int* 2008;102:1531-8)

An extended follow-up has been recently published (median 27.5 months), suggesting that degarelix might result in better progression-free survival compared to monthly leuprorelin which would mean longer prostate cancer control and a delay in the time when further therapies would need to be added. (Crawford ED, Tombal B, Miller K, Boccon-Gibod L, Schröder F, Shore N, et al. A phase III extension trial with a 1-arm crossover from leuprolide to degarelix: comparison of gonadotropin-releasing hormone agonist and antagonist effect on prostate cancer. J. Urol. 2011 Sep;186(3):889–97.)

Ongoing research suggests that degarelix may reduce the risk of further cardiovascular events in men who have suffered an event prior to commencing hormone therapy and this could potentially have a major impact on the overall morbidity, mortality and healthcare costs for men with advanced prostate cancer requiring androgen deprivation. (Smith MR, Klotz L, van der Meulen E, Colli E, Tankó LB.m J Urol. 2011 Nov;186(5):1835-42. doi: 10.1016/j.juro.2011.07.035. Epub 2011 Sep 25) (Tombal B, Albertsen P, de la Taille A, Malmberg A, Persson B-E, Olesen TK, Nilsson J. (2013). Lower risk of cardiovascular events in men receiving ADT by gonadotropin releasing hormone antagonist, degarelix, compared with luteinising hormone-releasing agonists. Poster presentation. European Association of Urology)

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

The following paper has recently submitted to and accepted by Eur Urol:
Cardiovascular Morbidity Associated with Gonadotropin Releasing Hormone Agonists and an Antagonist
Peter C Albertsen MD[1], Laurence Klotz MD[2], Bertrand Tombal MD[3], James Grady DrPH[1], Tine K Olesen MSc[4] Jan Nilsson MD[5]

<u>The authors would allow this paper to be released to NICE on a confidential basis as awaiting publication. It would seem appropriate for this paper to be considered in the final appraisal in order for there to be a full assessment of the potential reduction in cardiovascular morbidity associated with degarelix.</u>

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Also abstract from American Urology Association Meeting 2013

13-2094

Androgen deprivation therapy by a gonadotropin releasing hormone antagonist, degarelix, lowers the risk of cardiovascular events or death when compared to luteinising hormone-releasing agonists

Peter Albertsen, Farmington, CT, Bertrand Tombal, Brussels, Belgium, Thomas Wiegel, Ulm, Germany, Egbert van der Meulen, Copenhagen, Denmark, Bo-Eric Persson, Saint-Prex, Switzerland, Tine Kold Olesen, Copenhagen, Denmark, Joshua Beckman, Boston, MA*

INTRODUCTION AND OBJECTIVES: Patients treated with luteinising hormone-releasing hormone (LHRH) agonists for advanced prostate cancer are at an increased risk of cardiovascular (CV) events and related deaths. The gonadotropin releasing hormone (GnRH) antagonist, degarelix, appears to mitigate this risk.
METHODS: Data from 2328 patients participating in 6 prospective randomised trials comparing the GnRH antagonist,degarelix, (n=1491) to the GnRH agonists goserelin (n=458) or leuprolide (n=379) were pooled. Most patients (n=1686) received treatment for 1 year. Data were classified by the MedDRA system and analysed using Kaplan Meier plots and a Cox proportional hazard model. Event analysis was based on death from any cause or serious CV event (life threatening or requiring hospitalisation).High-risk patients were men with a prior history of CV disease (CVD) at baseline.
RESULTS: Baseline characteristics and prior CVD history (31% vs. 29%) were well balanced between treatment groups.Characteristics associated with CVD (e.g. statin medication, elevated blood pressure, diabetes, cholesterol >6.2 mmol/L) were also similar between groups.The analysis revealed one or more serious CV events or death from any cause for 78 patients. GnRH antagonist-treated men had a significantly lower risk of a serious CV event or death from any cause vs. men on an LHRH agonist (Table 1). Analysis of the risk of serious CV event for all patients showed a significantly lower risk for men receiving GnRH antagonist vs. LHRH agonist. The findings were greatest among high risk patients (Table 1). In patients with no baseline CVD, there was no difference in subsequent serious CV events or death in either group.
CONCLUSIONS: In comparison with LHRH agonists, the GnRH antagonist (degarelix) decreased the risk of subsequent serious CV event and serious CV event or death over one year of treatment in men with a history of CVD by more than 50%.
Source of Funding: Ferring Pharmaceuticals

Table 1. Hazard ratios for CV event or death: GnRH antagonist vs. LHRH agonists

	n	HR	95% CI	p-value
Serious CV event or death from any cause				
Entire population	2328	**0.593**	0.378-0.930	0.023
High risk patients	707	**0.414**	0.227-0.755	0.004
Serious CV event only				
Entire population	2328	**0.560**	0.318-0.988	0.046
High risk patients	707	**0.367**	0.174-0.775	0.009

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Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within
3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

Equality

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could lead to recommendations that have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.