National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Degarelix for treating advanced hormone-dependent prostate cancer

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	British Uro-oncology Group	Yes.	Comment noted. No changes to the remit required.
	Ferring Pharmaceuticals Ltd	Yes, this is an appropriate topic for NICE appraisal. Degarelix has already received a positive SMC appraisal and an AWMSG appraisal is underway at present. Currently in the absence of NICE guidance, cancer network and local guidance differs throughout the country leading to geographical variation in prescribing, inequality of access and local treatment strategies that are not evidence based.	Comment noted. No changes to the remit required.
	Prostate Cancer Support Federation	It is appropriate.	Comment noted. No changes to the remit required.
	Prostate Cancer UK	It would be appropriate to refer this topic to NICE.	Comment noted. No changes to the remit required.

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	Royal College of Pathologists	Please note that the Royal College of Pathologists does not see any great need for this drug. From what we have sourced and discussed with our clinical colleagues, it seems that it is not superior to what is available at the minute or cost effective. Also there is a higher rate of adverse local affects due to the injection. The only possible advantage is more rapid castrate testosterone levels than with LHRH agonists such as Zoladex. This might be useful for the one patient per year who presents with spinal cord compression as their first presentation of prostate cancer. Otherwise it is less convenient (once per month versus once every 3 months), more side effects (injection site reactions) and not any better than LHRH agonists.	Thank you for your comments. The Department of Health has issued NICE with a remit to appraise this drug so these issues will be considered during the course of the appraisal. No changes to the remit required.
Wording	British Uro-oncology Group	Yes.	Comment noted. No changes to the remit required.
	Ferring Pharmaceuticals Ltd	Yes	Comment noted. No changes to the remit required.
	Prostate Cancer Support Federation	Wording is correct.	Comment noted. No changes to the remit required.

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Timing Issues	AstraZeneca	Degarelix is currently available on the UK market since 2009 and therefore the urgency is lessened. Could the advice be incorporated into the upcoming CG 58?	The potential inclusion of degarelix was discussed during the scoping process for the update of CG58. It was decided that the topic should be entered into the Topic Selection process for Technology Appraisals and subsequently be scoped as a potential technology appraisal.
	British Uro-oncology Group	Degarelix Appraisal should be an urgent priority to ensure a spectrum of available therapies for this patient population.	Comment noted.
	Ferring Pharmaceuticals Ltd	There is a high priority associated with this NICE STA to place degarelix in the care pathway in the context of current care in NHS England. It is vital that the outcome of this appraisal is harmonised with the update of the prostate cancer clinical guidelines (CG58) both of which are required to help combat the current inconsistencies seen in prescribing practice and inequality in terms of patient access to treatment.	The Centre for Clinical Practice routinely considers references to published technology appraisal guidance where this is within the scope of the guideline and otherwise appropriate.

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	Prostate Cancer Support Federation	This is urgent, 30% of men diagnosed with prostate ccancer have metastatic disease and this is an imortant new drug to help them.	Comment noted.
	Prostate Cancer UK	Prostate Cancer UK welcomes NICE's proposed Single Technology Appraisal of degarelix. Should the proposed appraisal recommend that this agent is effective, it will help to provide standardised access and increased patient choice to these patients.	Comment noted.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	British Uro-oncology Group	The information is generally satisfactory	Comment noted. No changes to the scope required.
	Ferring Pharmaceuticals Ltd	Please confirm that the definition of 'advanced' prostate cancer is a tumour that has spread beyond the prostatic capsule (i.e. locally advanced or metastatic). It might also be worth specifying some of the unwanted effects of testosterone flare such as bone pain, LUTS & spinal cord compression (Klotz et al BJU Int 2008) as these result in additional costs to the NHS as a whole and have a negative impact on patients HR-QoL	Thank you for your comments. The background section has been amended to confirm that advanced disease means prostate cancer that has spread beyond the prostatic capsule. The manufacturer will be able to outline the potential health-related benefits as part of its evidence submission.

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	NRCI	Paragraph 3: Treatment with GnRH agonist is recommended before, during and after radical radiotherapy (total duration 6 -9 months) for patients with intermediate risk localised prostate cancer. Patients with high risk prostate cancer (T3a/b or T4 disease, Gleason score >7 and /or PSA > 20) should receive adjuvant hormone therapy for a total duration of 3 years, starting before radiotherapy. Patients who locally advanced disease unfit for radical local treatment or who present with lymph node positive or metastatic disease are treated primarily with long-term GnRH therapy. Anti-androgens (bicalutamide) or orchidectomy is an alternative for selected patients. Paragraph 4: bilateral orchidectomy is not an option for patients with impending cord compression as they require urgent radiotherapy or surgery to prevent spinal cord damage which would be delayed by an orchidectomy.	Thank you for your comments. The background section has been amended to include bicalutamide because this has been added to the scope as a comparator following feedback from consultees and commentators. The European Association of Urologists prostate cancer guideline gives bilateral orchidectomy as an example of an alternative treatment strategy for people with impending spinal cord compression. No change to the scope required.
	Prostate Cancer Support Federation	Accurate.	Comment noted. No changes to the scope required.
	Prostate Cancer UK	Prostate Cancer UK note that in the background section reference is made to 'around 55-65% of people with prostate cancer develop metastatic disease'. We believe it would be helpful if primary evidence could be provided. It is also important to note that the National Horizon Scanning Centre and CancerHelp UK now state that "metastatic disease occurs in 20-30% of men with prostate cancer". The background information does not cover the treatment for men with advanced prostate cancer at diagnosis, for whom hormonal therapies are usually presecribed as first-line therapies.	Cancer Research UK statistics show that approximately 20-30% of men with primary prostate cancer *present* with incurable metastatic disease in the UK (that is, have metastatic disease at diagnosis rather than over the course of the disease). No change to the scope required.

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	Royal College of Physicians	Paragraph 3: Treatment with GnRH agonist is recommended before, during and after radical radiotherapy (total duration 6 -9 months) for patients with intermediate risk localised prostate cancer. Patients with high risk prostate cancer (T3a/b or T4 disease, Gleason score >7 and /or PSA > 20) should receive adjuvant hormone therapy for a total duration of 3 years, starting before radiotherapy. Patients who locally advanced disease unfit for radical local treatment or who present with lymph node positive or metastatic disease are treated primarily with long-term GnRH therapy. Anti-androgens (bicalutamide) or orchidectomy is an alternative for selected patients. Paragraph 4: bilateral orchidectomy is not an option for patients with impending cord compression as they require urgent radiotherapy or surgery to prevent spinal cord damage which would be delayed by an orchidectomy.	Thank you for your comments. The background section has been amended to include bicalutamide because this has been added to the scope as a comparator following feedback from consultees and commentators. The European Association of Urologists prostate cancer guideline gives bilateral orchidectomy as an example of an alternative treatment strategy for people with impending spinal cord compression. No change to the scope required.
The technology/ intervention	British Uro-oncology Group	The information is generally satisfactory	Comment noted. No changes to the scope required.
	Ferring Pharmaceuticals Ltd	Please confirm the definition of "Advanced Prostate Cancer" as above - 'spread beyond the prostate' could imply metastatic disease only. In contrast to LHRH agonists, the rapid testosterone suppression following degarelix administration results in immediate castration, and as such degarelix represents the closest pharmacological substitute for orchidectomy (Brawer MK et al, Rev Urol 2001).	Thank you for your comment. The background section has been amended to confirm that advanced disease means prostate cancer that has spread beyond the prostatic capsule.
	NRCI	yes	Comment noted. No changes to the scope required.

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	Prostate Cancer Support Federation	*Is the description of the technology or technologies accurate?* Yes.	Comment noted. No changes to the scope required.
	Prostate Cancer UK	*Is the description of the technology or technologies accurate?* Yes	Comment noted. No changes to the scope required.
	Royal College of Physicians	*Is the description of the technology or technologies accurate?* Yes	Comment noted. No changes to the scope required.
Population	British Uro-oncology Group	This is in accordance with the clinical trials	Comment noted. No changes to the scope required.
	Ferring Pharmaceuticals Ltd	Ferring Pharmaceuticals agree that the principal population to be considered is patients with advanced hormone-dependent prostate cancer (defined as cases that have spread beyond the prostatic capsule). A key sub-group is high risk patients who have a PSA of >20ng/ml. In addition, there are sub-populations where current alternative therapies are inappropriate because of associated risks such as tumour flare and side-effects. These subgroups include: - Patients with high-risk advanced hormone-dependent prostate cancer where a testosterone surge is likely to negatively impact on their disease, such as those with: - Spinal metastases with impending or actual spinal cord compression - High tumour volume with impending or actual urinary outflow obstruction - Bony metastases associated with intractable pain. - Patients who are currently treated with warfarin or CYP450 operators or who have reduced liver function, for whom standard anti-androgen treatment is contraindicated. For example, it is recommended that patients on bicalutamide who are receiving concomitant warfarin should have close monitoring of prothrombin time. This would not be a problem for patients receiving degarelix which is not a substrate for the CYP450 system and who do not require anti-	Thank you for your comments. The population in the draft scope has been amended to be clear that it refers to disease that has spread beyond the prostatic capsule (including biochemical relapse). Scoping workshops agreed that there are subgroups that could derive particular benefit from avoiding testosterone flare, or in whom other hormonal therapies are contraindicated. The scope has been amended to state that, if evidence allows, the following subgroups will be considered: high-risk patients with PSA >20 ng/mL; patients with spinal metastases with

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		androgen flare protection. - Patients at risk of evolving cardiovascular co-morbidity. In men with prostate cancer observed rates of cardiovascular disease events were similar before and after initiation of degarelix treatment (Smith M et al. 2011).	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.
	NRCI	There is evidence that patiens with more advanced disease (Tombal et al Eur Urol 2010; 57;836) have better PSA control and survival; patients with significant obstructive symptoms (Axcrona BJU INT 2012 Epub; Mason et al Clin Onc in press) have better symptom control and quality of life with degarelix. Related costs to improve urinary obstruction (TURP, alpha blockers) should be considered. There is no published evidence for paitents with impending or estabished cord compression. However, these patients also receive high dose dexamethasone and radiotherapy or surgery at diagnosis; it is likely that these additional treatments reduce the tumour size and pressure on the spinal cord more than hormone therapy initially. There is limited clinical evidence as cord compression as presenting symptom affects only a small number of patients and requires urgent intervention which makes a randomised trial difficult.	Comment noted. The appraisal will take account of the available evidence. No changes to the scope required.
	Prostate Cancer Support Federation	*Is the population defined appropriately? Are there groups within this population that should be considered separately?* All correct.	Comment noted. No changes to the scope required.
	Prostate Cancer UK	Prostate Cancer UK believes this population has been correctly defined.	Comment noted. No changes to the scope required.

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	Royal College of Physicians	There is evidence that patiens with more advanced disease (Tombal et al Eur Urol 2010; 57;836) have better PSA control and survival; patients with significant obstructive symptoms (Axcrona BJU INT 2012 Epub; Mason et al Clin Onc in press) have better symptom control and quality of life with degarelix. Related costs to improve urinary obstruction (TURP, alpha blockers) should be considered. There is no published evidence for paitents with impending or estabished cord compression. However, these patients also receive high dose dexamethasone and radiotherapy or surgery at diagnosis; it is likely that these additional treatments reduce the tumour size and pressure on the spinal cord more than hormone therapy initially. There is limited clinical evidence as cord compression as presenting symptom affects only a small number of patients and requires urgent intervention which makes a randomised trial difficult.	Comment noted. The appraisal will take account of the available evidence. No changes to the scope required.
Comparators	AstraZeneca	We would suggest individually specifying GnRH agonists as they have different therapeutic indications and supporting evidence base. We would also recommend including as comparators, GnRH agonists in combination with an anti-androgen to reduce testosterone flare as seen in clinical practice.	Thank you for your comments. During consultation it was established that GnRH agonists are perceived to have a class effect but that they differ in price so the scope has been amended to specify the drugs individually. Consultees and commentators indicated that an anti-androgen is routinely used in clinical practice in combination with a GnRH agonist to treat testosterone flare at initiation of treatment. Therefore, the scope has been updated to state that GnRH agonists are used in combination with short-term anti-androgen therapy.

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	British Uro-oncology Group	The comparator is appropriate. It could be noted that goserelin and leuprolelin are the most commonly used agonists, but generally it is believed that there is a class effect for GnRH agonists. Anti-androgens would not be an appropriate comparator as this would be a different class of action. Furthermore, the most commonly anti-androgen used as monotherapy is bicalutamide and this was shown to be inferior to LHRH agonists in a clinical trial and is not licenced for advanced (metastatic) disease. Bilateral orchidectomy would also be an inappropriate comparator, given that in clinical trials, orchidectomy was the comparator for GnRH agonists and GnRH agonists were shown to be clinically equivalent.	Thank you for your comments. During consultation it was established that GnRH agonists are perceived to have a class effect but that they differ in price so the scope has been amended to specify the drugs individually. During consultation it was established that bicalutamide is used in routine clinical practice to treat a subgroup of patients with advanced prostate cancer. Therefore, bicalutamide can be considered an appropriate comparator and has been added to the scope. Consultees and commentators agreed that bilateral orchidectomy was not a comparator because patients would have to make a decision between surgical and pharmacological intervention before deciding which particular drug would best suit their needs. Therefore, bilateral orchidectomy has not been added to the scope.
	Ferring Pharmaceuticals Ltd	HRH agonists (with addition of an anti-androgen to manage testosterone flare) are the standard comparative treatments. Current literature and clinical practice observations indicate there is a class effect observed for all LHRH agonists	Thank you for your comments. During consultation it was established that GnRH

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		(Evans et al. 2005). Data collected for degarelix used leuprorelin as the comparator. Anti-androgens alone should not be considered as comparators since they are infrequently used as first line monotherapy. However they should be considered as a combination treatment with LHRH agonists to manage testosterone flare. Orchidectomy should not be considered as a comparator as the standard of care is pharmacological intervention rather than surgical.	agonists are perceived to have a class effect but that they differ in price so the scope has been amended to specify the drugs individually. During consultation it was established that bicalutamide is used in routine clinical practice to treat a subgroup of patients with advanced prostate cancer. Therefore, bicalutamide can be considered an appropriate comparator and has been added to the scope. Consultees and commentators indicated that an anti-androgen is routinely used in clinical practice in combination with a GnRH agonist to treat testosterone flare at initiation of treatment. Therefore, the scope has been updated to state that GnRH agonists are used in combination with short-term anti-androgen therapy. Consultees and commentators agreed that bilateral orchidectomy was not a comparator because patients would have to make a decision between surgical and pharmacological intervention

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			before deciding which particular drug would best suit their needs. Therefore, bilateral orchidectomy has not been added to the scope.
	NRCI	bicalutamide should be included as comparator	Thank you for your comment. During consultation it was established that bicalutamide is used in routine clinical practice to treat a subgroup of patients with advanced prostate cancer. Therefore, bicalutamide can be considered an appropriate comparator and has been added to the scope.
	Prostate Cancer Support Federation	*Is this (are these) the standard treatment(s) currently used in the NHS with which the technology should be compared? Can this (one of these) be described as 'best alternative care'?* Yes.	Comment noted. No changes to the scope required.

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	Prostate Cancer UK	Prostate Cancer UK believes the comparitors should be LHRH agonists and orchidectomy. We believe it is not possible to compare anti androgens with degarelix.	Thank you for your comment. During consultation it was established that bicalutamide is used in routine clinical practice to treat a subgroup of patients with advanced prostate cancer. Therefore, bicalutamide can be considered an appropriate comparator and has been added to the scope. Consultees and commentators agreed that bilateral orchidectomy was not a comparator because patients would have to make a decision between surgical and pharmacological intervention before deciding which particular drug would best suit their needs. Therefore, bilateral orchidectomy has not been added to the scope.

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	Royal College of Physicians	Bicalutamide should be included as comparator	Thank you for your comment. During consultation it was established that bicalutamide is used in routine clinical practice to treat a subgroup of patients with advanced prostate cancer. Therefore, bicalutamide can be considered an appropriate comparator and has been added to the scope.
Outcomes	British Uro-oncology Group	Yes	Comment noted. No changes to the scope required.
	Ferring Pharmaceuticals Ltd	In-line with some other therapies in this indication and because PSA is a good indicator of biochemical disease progression, time to PSA progression and PSA Progression Free Survival (PFS) are the most relevant outcomes used due to the extended time horizon (Smith et al. 1997, Scher et al. 1999). Overall survival rate was not considered as a primary outcome for degarelix.	Thank you for your comment. During consultation it was established that time to PSA progression and PSA progression-free survival were appropriate outcomes for consideration and have been added to the scope.
	NRCI	yes	Comment noted. No changes to the scope required.
	Prostate Cancer Support Federation	*Will these outcome measures capture the most important health related benefits (and harms) of the technology?* Yes.	Comment noted. No changes to the scope required.

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	Prostate Cancer UK	The relevant clinical outcomes we would identify are those already set out in the draft scope. However, it is important that health-related quality of life and adverse effects are considered with an equal standing to the other outcomes. Patient-reported outcomes should also be considered, to ensure that the agent is not only clinically effective but also improves outcomes of importance to this patient population. Aspects that relate to quality of life should be specifically considered, including the impact of the treatment regimen on number of hospital appointments, method of delivering treatment (e.g. oral, intravenous etc.) and side effects.	Comment noted. Committee will give all outcomes due consideration during the appraisal. No changes to the scope required.
	Royal College of Physicians	Yes	Comment noted. No changes to the scope required.
Economic analysis	AstraZeneca	The time horizon should reflect the lifetime of the patient who has progressed to advanced hormone-dependant prostate cancer.	Comment noted. No changes to the scope required.
	Ferring Pharmaceuticals Ltd	The model will be developed with a lifetime time horizon to reflect the long term benefits of delaying PSA progression on costs associated with later stage treatment and quality of life. Shorter time horizons reflecting the trials will be examined in sensitivity analysis which includes 5 year data from a long term follow up RCT where the 3 year data is published in an interim analysis (Crawford J Urol 2011)	Comment noted. No changes to the scope required.
	NRCI	none	Comment noted. No changes to the scope required.
	Prostate Cancer Support Federation	*Comments on aspects such as the appropriate time horizon* None.	Comment noted. No changes to the scope required.
	Prostate Cancer UK	We do not have enough evidence to comment of this area.	Comment noted. No changes to the scope required.
	Royal College of Physicians	None	Comment noted. No changes to the scope required.

Section	Consultees	Comments	Action
Equality and Diversity	Prostate Cancer Support Federation	No equality issues.	Comment noted. No changes to the scope required.
	Ferring Pharmaceuticals Ltd	No changes required	Comment noted. No changes to the scope required.
	Prostate Cancer UK	It will be important to ensure that access to this technology is equitable and discrimination does not occur solely on the basis of age, ethnicity or socio-economic status. Prostate cancer is more common in men aged over 60 and African Caribbean men are three times more likely to develop prostate cancer than white men of the same age in the UK. Eligible patients from these populations should not be denied access to this technology (if approved) because of factors related to their age, ethnicity and socio-economic status. Information and communication strategies must also be considered and patients consulted to ensure that access can be as equitable as possible.	Comment noted. No changes to the scope required.
Innovation	AstraZeneca	While degarelix offers a new mechanism of action, it is unclear what benefits prostate cancer patients can expect to recieve.	Thank you for your comments. Aspects of innovation should be described in the evidence submissions. The Committee will consider the innovative nature of degarelix during the course of the appraisal. No amendment to the scope required.

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	Ferring Pharmaceuticals Ltd	Degarelix is the only gonadotrophin-releasing hormone (GnRH) antagonist licensed in the UK for the treatment of advanced hormone-dependent prostate cancer and provides a monotherapy approach to the management of prostate cancer. In contrast to LHRH agonists, degarelix acts by blocking GnRH receptors. Through this direct mechanism of action, degarelix rapidly produces a profound reduction in testosterone to castration levels, without any initial surge in hormone levels, thereby avoiding the risk of clinical flare and the need for concomitant anti-androgen therapy. This therapy outcome is particularly important for the more severely affected patients, who may require immediate suppression of testosterone without flare. Degarelix provides an effective and close pharmacological substitute to orchidectomy and hence, degarelix is a step-change in the management of advanced hormone-dependent prostate cancer. The axial skeleton is affected in a high proportion of patients who die from prostate cancer (Lecouvet et al. 2010) and the presence and extent of bone metastases can reflect prognosis. Degarelix may improve the control of skeletal metastases (as indicated by the serum alkaline phosphatase [ALP] marker). Comparator evidence suggest that degarelix may offer improved serum ALP control, especially in patients with metastatic disease or baseline PSA levels ≥50 ng/ml (Schroder et al. 2009) when compared to leuprorelin. These observations support the hypothesis that degarelix may further prolong control of skeletal metastases compared with LHRH agonists during long-term treatment. It is worth pointing out that in the degarelix phase III study (Klotz et al BJU Int 2008) of the patients in the leuprorelin group who received bicalutamide as flare protection, 74% still had a testosterone surge, 81% of those who did not receive bicalutamide in the leuprorelin group had a testosterone surge and none of those receiving degarelix had a testosterone surge. In addition, while not a primary endpoint of the Phase III trial (Klotz BJU 2008) and its extension (Crawford J Urol 2011) PSA PFS was superior with degarelix compared to leuprorelin.	Thank you for your comments. Aspects of innovation should be described in the evidence submissions. The Committee will consider the innovative nature of degarelix during the course of the appraisal. No amendment to the scope required.

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	Prostate Cancer Support Federation	Degarelix is a hormone treatment which works in much the same way as Zoladex by suppressing the body's production of testosterone. It's advantage over other treatments is that, when it is first given, it does not produce the testosterone flare, which is caused by Zoladex and the patient does not have to be given drugs such as Cyproterone acetate at the start of treatment. Degarelix starts to work on lowering testosterone levels immediately which also reflects quickly on PSA levels. In the long term, it has been shown to be beneficial for a longer time than alternative treatments.	Thank you for your comments. Aspects of innovation should be described in the evidence submissions. The Committee will consider the innovative nature of degarelix during the course of the appraisal. No amendment to the scope required.
	Prostate Cancer UK	Yes.	Comment noted. No changes to the scope required.
Other considerations	Ferring Pharmaceuticals Ltd	Ferring suggest that the development of NICE STA for degarelix is considered in the context of the development of the NICE CG58 and that subsequent recommendations are harmonised.	The Centre for Clinical Practice routinely considers references to published technology appraisal guidance where this is within the scope of the guideline and otherwise appropriate.
	Prostate Cancer Support Federation	A screening programme would make this drug less necessary.	Comment noted. No changes to the scope required.
	Prostate Cancer UK	The Scottish Medicines Consortium (SMC) approved the use of degarelix for men with advanced hormone-dependent prostate cancer in January 2011 under a patient access scheme with the manufacturer.	Comment noted. No changes to the scope required.
Questions for consultation	AstraZeneca	Comparators Question 1: The common GnRH agonists in use in UK are goserelin, leuprorelin and triptorelin used in combination with anti-androgen 3 days before and 3 weeks after initiation.. We believe that they should be individually specified as comparators since the indication and supporting evidence base from section 5.1 of their respective SmPCs are significantly different. They	Thank you for your comments. During consultation it was established that GnRH agonists are perceived to have a class effect but that they differ in price so the scope has been amended to specify the

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		should be considered to be always co-adminsitered with an anti-androgen and the incidence of testosterone flare should reflect this. Question 2: Bicalutamide 150mg is only licensed for locally advanced prostate cancer and therefore wouldn't be appropriate for the population specified in the scope. Question 3: Bilateral orchidectomies have significantly reduced since the introduction of GnRH agonists, but are still used in clinical practice and therefore relevant as a comparator. Subgroups Question 1: As discussed in the GnRH agonists' SmPCs, initial use of an anti-androgen for 3 days before and 3 weeks after the commencement of GnRH agonist can avoid the initial flare of testosterone levels so we would query whether this subgroup is appropriate in clinical practice. Equality As discussed in the background, The incidence of prostate cancer increases with age and is higher in men of African-Caribbean family origin. therefore if this medicine is not approved, it may disadvantage men of African-Caribbean origin and elderly men.	drugs individually. Consultees and commentators indicated that an anti-androgen is routinely used in clinical practice in combination with a GnRH agonist to treat testosterone flare at initiation of treatment. Therefore, the scope has been updated to state that GnRH agonists are used in combination with short-term anti-androgen therapy. During consultation it was established that bicalutamide is used in routine clinical practice to treat a subgroup of patients with advanced prostate cancer. Therefore, bicalutamide can be considered an appropriate comparator and has been added to the scope. Consultees and commentators agreed that bilateral orchidectomy was not a comparator because patients would have to make a decision between surgical and pharmacological intervention before deciding which particular drug would best suit their needs. Therefore, bilateral orchidectomy has not

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			been added to the scope. Equality in accessing a technology will be considered during the course of the appraisal. No change to the scope required.
	Ferring Pharmaceuticals Ltd	Questions for consultation stated in the draft scope regarding comparators and subgroup of people in whom the technology is expected to be more effective have been addressed in the above sections	Comment noted. See above sections for response.
	NCRI	Which GnRH agonists are most commonly used in clinical practice and should these be individually specified as comparators: Goserelin, leuprorelin and triptorelin are all GnRH analogues and commonly used; the effectiveness and toxicity is the similar. Triptorelin is slightly cheaper and can be given as 6 month injection. Anti-androgens are used as alternative for short term neo-adjuvant therapy, patients with loclised disease or patients with a history of cardio-vascular problems. From the evidence it seems that degarelix is more effective for men with a high tumour load or significant urinary symptoms, so a different population. orchidectomy is rarely used; most men prefer non-surgical castration even if it might be a more cost effective alternative. It is not suitable for short term adjuvant therapy.	Thank you for your comments. During consultation it was established that GnRH agonists are perceived to have a class effect but that they differ in price so the scope has been amended to specify the drugs individually.
	Prostate Cancer Support Federation	*Please answer any of the questions for consultation if not covered in the above sections. If appropriate, please include comments on the proposed process this appraisal will follow (please note any changes made to the process are likely to result in changes to the planned time lines).* None	Comment noted. No changes to the scope required.

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	Prostate Cancer UK	Prostate Cancer UK is only aware of this technology, so we do not see what other GnRH agonists it can be compared with. Prostate Cancer UK believes that degarelix could derive a particular clinical benefit from avoiding an initial flare of testosterone levels in men with advanced hormone-dependent prostate cancer.	Comment noted. No changes to the scope required.
	Royal College of Physicians	Which GnRH agonists are most commonly used in clinical practice and should these be individually specified as comparators: Goserelin, leuprorelin and triptorelin are all GnRH analogues and commonly used; the effectiveness and toxicity is the similar. Triptorelin is slightly cheaper and can be given as 6 month injection. Anti-androgens are used as alternative for short term neo-adjuvant therapy, patients with loclised disease or patients with a history of cardio-vascular problems. From the evidence it seems that degarelix is more effective for men with a high tumour load or significant urinary symptoms, so a different population. orchidectomy is rarely used; most men prefer non-surgical castration even if it might be a more cost effective alternative. It is not suitable for short term adjuvant therapy.	Thank you for your comments. During consultation it was established that GnRH agonists are perceived to have a class effect but that they differ in price so the scope has been amended to specify the drugs individually. Consultees and commentators indicated that an anti-androgen is routinely used in clinical practice in combination with a GnRH agonist to treat testosterone flare at initiation of treatment. Therefore, the scope has been updated to state that GnRH agonists are used in combination with short-term anti-androgen therapy. During consultation it was established that bicalutamide is used in routine clinical practice to treat a subgroup of patients with advanced prostate cancer. Therefore, bicalutamide can be considered an appropriate

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			comparator and has been added to the scope. Consultees and commentators agreed that bilateral orchidectomy was not a comparator because patients would have to make a decision between surgical and pharmacological intervention before deciding which particular drug would best suit their needs. Therefore, bilateral orchidectomy has not been added to the scope.
Additional comments on	British Uro-oncology Group	BUG fully supports the availability of degarelix for clinical practice.	Comment noted. No changes to the scope required.

Section	Consultees	Comments	Action
the draft scope.	Ferring Pharmaceuticals Ltd	References: Brawer MK, Crawford ED, Labrie F, Mendoza-Valdes A, Miller PD, Petrylak DP. Androgen deprivation and other treatments for advanced prostate cancer. Rev Urol. 2001;3 Suppl 2:S59-68. Crawford DE, Tombal B, Miller K, Boccon-Gibod L, Schröder F, 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; 186: 889-897. Evans CP, Fleshner N, Fitzpatrick JM, Zlotta AR. An evidence-based approach to understanding the pharmacological class effect in the management of prostatic diseases. BJU Int. 2005 Apr;95(6):743-9. Klotz L, Boccon-Gibod L, Shore ND, Andreou C, Persson B, 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. Br J Urol Int 2008; 1531-1538. Lecouvet FE, Simon M, Tombal B et al. Whole-body MRI (WB-MRI) versus axial skeleton MRI (AS-MRI) to detect and measure bone metastases in prostate cancer (PCa). Eur Radiol 2010; 20: 2973–2982. Scher HI, Kelly WM, Zhang ZF, Ouyang P, Sun M, Schwartz M, Ding C, Wang W, Horak ID, Kremer AB. Post-therapy serum prostate-specific antigen level and survival in patients with androgen-independent prostate cancer. J Natl Cancer Inst. 1999 Feb 3;91(3):244-51. Schroder FH, Tombal B, Miller K et al. Changes in alkaline phosphatase levels in patients with prostate cancer receiving degarelix or leuprolide: results from a 12-month, comparative, phase III study. BJU Int 2009; 106: 182–187. Smith JA Jr, Lange PH, Janknegt RA, Abbou CC, deGery A. Serum markers as a predictor of response duration and patient survival after hormonal therapy for metastatic carcinoma of the prostate. J Urol. 1997. April; 157(4):1329-34 Smith M, Klotz L, van der Meulen E, Colli E, Tanko LB. Gonadotropin-Releasing Hormone Blockers and Cardiovascular Disease Risk: Analysis of Prospective Clinical Trials of Degarelix. J Urol 2011; 186: 1835–1842.	These references have been noted. The manufacturer should supply copies of supporting references as part of its evidence submission.

Section	Consultees	Comments	Action

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Department of Health
MHRA
Royal College of Nursing

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Degarelix for treating advanced hormone-dependent prostate cancer

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral)

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
	Proposal:	Proposal made by:		Action taken: Removed/Added/Not included/Noted	Justification:
1.	Add NHS England	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. NHS England has been included in the matrix of consultees and commentators under 'other consultees.'
2.	Move British Prostate Group to 'Professional Group-consultees'	NICE Secretariat		Added	This organisation has been re-classified as a 'Professional Group- consultee'.

3.	Add Independent Cancer Patient's Voice	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Independent Cancer Patient's Voice has been included in the matrix of consultees and commentators under 'patient groups.'
4.	Add Urology Foundation	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Urology Foundation has been included in the matrix of consultees and commentators under 'professional groups.'

5.	Add Health Research Authority	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Health Research Authority has been included in the matrix of consultees and commentators under 'research groups.'
6.	Remove Prostate Action	NICE Secretariat and Prostate Cancer UK		Removed	This organisation has merged with Prostate Cancer UK who are already on the matrix under 'patient groups.'
7.	Remove Association of Surgeons of Great Britain and Ireland	NICE Secretariat		Removed	This organisation's interests are not closely related to the appraisal topic and as per our inclusion criteria. Association of Surgeons of Great Britain and Ireland has been removed from the matrix.

8.	Remove Royal College of Surgeons	NICE Secretariat		Removed	This organisation's interests are not closely related to the appraisal topic and as per our inclusion criteria. Royal College of Surgeons has been removed from the matrix.
9.	Remove North Yorkshire & York PCT Cluster	NICE Secretariat		Removed	This organisation has disbanded.
10.	Remove The Humber PCT Cluster	NICE Secretariat		Removed	This organisation has disbanded.
11.	Add Public Health England	NICE Secretariat		Added	This organisation's interests are closely related to the appraisal topic and as per our inclusion criteria. Public Health England has been added to the matrix of consultees and commentators under 'Associated Public Health Group – commentators.'
12.	Move Public Health Wales NHS Trust to 'Associated Public Health Group - commentators'	NICE Secretariat		Added	This organisation has been re-classified as 'Associated Public Health Group - commentators'.

13.	Add NHS Durham Dales, Easington and Sedgefield CCG	NICE Secretariat		Added	Our process requires the involvement of two CCGs/LHBs. Therefore NHS Durham Dales, Easington and Sedgefield CCG is now included on the matrix.
14.	Add NHS Southport and Formby CCG	NICE Secretariat		Added	Our process requires the involvement of two CCGs/LHBs. Therefore NHS Southport and Formby CCG is now included on the matrix.