Comments on the ACD Received from the Public through the NICE Website

Name	[redacted]
Role	NHS Professional
Other role	Prostate cancer patient
Location	England
Conflict	yes
Notes	I am a cardiologist, and saw the dramatic improvements in cvs outcomes with degarelix versus LHRH agonists, and was so struck by the better outcome with degarelix that I engaged with the manufacturer further. I strongly feel that using degarelix rather than LHRH agonists will save lives, and have spoken to this effect at meetings sponsored by Ferring
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I disagree entirely with the NICE conclusions; degarelix has fewer CVS risks than LHRH agonists, and my calculations suggest that the NICE recommendation in effect to continue using LHRH agonists rather than degarelix will result in some 3,500 excess CVS events per year in the UK, including heart attack and death. As a consultant cardiologist I am very interested in any possible cardiac side effects of any treatment, especially anti-cancer treatment. There have been multiple trials raising concerns over LHRH agonists, so much so that 4 eminent American medical societies (including the American Heart Association and American Cancer Society) in 2010 issued a scientific advisory greatly raising concerns about the cardiovascular risk factor side effect profile of LHRH agonists. These were most likely in those with pre-existing cardiovascular disease (about 1/3 of prostate cancer patients). This is worrying, and requires serious thought and study for prevention. The cardiovascular data on degarelix versus LHRH agonist is sufficiently compelling to believe, and adopt as the default position. If NICE do not do so, the likelihood is that patients will die needlessly.
Section 2 (The technology)	The finding in 1941 that prostate cancer is a hormone dependent cancer (testosterone) led to Huggins receiving the Nobel prize in 1966. This was a key advance in the management of prostate cancer and led to an understanding that testosterone removal/receptor blockade was vital to the successful management of this condition. A drug such as degarelix that immediately and massively lowers testosterone levels is scientifically very attractive. Conversely, any drug that increase testosterone levels must be avoided at all costs. It is therefore bizarre in the extreme that the LHRH agonists, which produce a massive surge of testosterone at initiation, only partially blocked by testosterone antagonists given by some oncologists some of the time, are in any sense a recommended therapy. Intellectually, using GnRH antagonists to block testosterone production is an elegant way of lowering testosterone levels, and does so without producing a tumour enhancing hormone flair. This is particularly the case as we know that any testosterone receptor blocking drug is only

	partially effective, and can in no way fully counteract the tumour enhancing testosterone flair resulting from LHRH agonists.
Section 3 (The manufacturer's submission)	As a cardiologist I am interested in CVS risk generally, and particular in cancer and its treatment. Prostate cancer is particularly relevant as patients are already at high risk of CVS events (men, elderly), and some 1/3 have pre-existing CVS disease. Anything that increases risk, even if marginally, given the high pre-existing risk will be very detrimental. There is a strong steer from the data that LHRH agonists increase CVS risks, especially in those with pre-existing CVS disease. The risk is about 60% lower with degarelix, according to the data of Bertrand Tombal et al. Put another way, in those with CVS disease the risk of a serious CVS event at 1 year on LHRH agonists is about 12%, with degarelix 5%, an absolute risk difference of 7%. With some 150,000 patients receiving LHRH agonists in the UK, and 1/3 with CVS disease, there will be (50,000 x 0.07) about 3,500 fewer serious CVS event will occur if degarelix is used rather than the inelegant LHRH agonists.
Section 4 (Consideration of the evidence)	I cannot see the rationale for NICE supporting a drug that increases testosterone levels at a mission critical stage of a hormone responsive illness. NICE have failed to present evidence that testosterone receptor blockers are used universally, or are 100% effective. There is accumulating evidence that the testosterone flair may translate into LHRH agonists being less effective anti-cancer drugs than the GnRH antagonist degarelix. NICE also has not produced evidence that patients are fully informed about the LHRH testosterone flair. Finally, as a cardiologist, I am very impressed with the power of the pooled analysis by Bertrand Tombal et al that degarelix has fewer CVS side effects than LHRH agonists. NICE may not like pooled analyses, but we live in an imperfect world; the data is good, and we should go with this. If NICE gets this wrong, there will be 35,000 patients (at 10 years) with unnecessary heart attacks and CVS death. If degarelix were more expensive than the alternatives, then one could titrate cost against gain; my understanding is that there is no difference in cost, and NICE is therefore compelled to go with the drug with the safer side effect profile.
Section 5 (Implementation)	Patients must be given choice in their health care treatments, particularly for emotive diseases such as cancer. For choice to mean anything patients must be informed of the therapeutic benefit and side effect profile of alternative treatments. Patients must be informed of the testosterone flair with LHRH agonists (and that fact that prostate cancer is stimulated by testosterone) and the risks of this. They should be offered a drug without a flair, if choice in the NHS is to mean anything at all. Furthermore, patients with CVS disease must be told of the highly suggestive data informing us that degarelix has less CVS risk than LHRH agonists. If choice matters, then NICE must support this and support degarelix. If they do not, then NICE have clearly positioned themselves as not supporting patient choice, and by extension, if you have no choice over your treatment, then there is no role for patient education in prostate cancer. This would be a sad day, it would position NICE as an

	organisation which might pay lip service to modernity in the NHS, but which is essentially old fashioned authoritarian and paternalistic.
Section 6 (Proposed recommendations for further research)	No comment
Section 7 (Related NICE guidance)	No comment
Section 8 (Proposed date of review of guidance)	No comment
Date	16/01/2014 23:18:00

Name	[redacted]
Role	NHS Professional
Location	England
Conflict	no
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	There is a problem with recommendation 1.1. Â I would really want to start treatment on a man with a very high PSA when I first met him. Â I would not wait for bone or other scans. Â Men with a Â very high PSA should be considered for degarelix immediately, not after MR or bone scans show impending spinal cord compression. Â In addition, patients presenting with renal failure due to ureteric compression should be eligible.
Section 3 (The manufacturer's submission)	I am not sure why the ERG feel that cardiovascular events would be the same in degarelix and LHRH treated patients. Â I appreciate that the differences in cardiovascular events was shown in a post hoc analysis of pooled data, which is not ideal, but, on a balance of probabilty, it is extremely likely that cardiovascular risk is lower in degarelix treated patients.
Date	10/01/2014 11:19:00

Name	[redacted]
Role	NHS Professional
Location	England
Conflict	no
Notes	I have received honoraria for being on advisory board for the manufacturer
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	There are other patients who would benefit for this medication not just spinal mets. Patients with bone pain (in other areas) benefit and are often pain free 10 days after starting this treatment. POatients with high disease burden (e.g. very high PSA) benefit.

	Patients with post renal failure/hydronephrosis benefit as this is often releived after starting this treatment. Patients with significant cardiac co-morbidities have been shown to benefit. I beleive restricting this medicine to 'only spinal mets' is wrong.
Section 8 (Proposed date of review of guidance)	No oncology or urology representative
Date	07/01/2014 09:31:00