Review of TA404; Degarelix for treating advanced hormone-dependent prostate cancer

TA404 was published in August 2016 and scheduled to be considered for review in June 2019.

Proposal

The guidance should be transferred to the ‘static guidance list’.

Rationale

TA404 includes an optimised recommendation of degarelix for people with advanced hormone-dependent prostate cancer and spinal metastases. It concluded that degarelix was cost-effective in this subgroup of people with spinal metastases and that these patients were more likely to benefit because the risk of developing spinal compression was higher. The committee’s preferred ICERs comparing degarelix with luteinising hormone-releasing hormone (LHRH agonist; leuprorelin, goserelin and triptorelin) for this subgroup were all below £30,000 per QALY gained whereas its preferred ICERs for the full population were above the range normally considered a cost-effective use of NHS resources.

The cost-effectiveness results included a discounted price for degarelix (a national branded framework agreement with the Commercial Medicines Unit for secondary care, and a commercial scheme available to clinical commissioning groups for primary care). TA404 only recommends degarelix if it is available at the same discounted cost that was available in 2016. The company has confirmed that this discount is still in place. Furthermore, there have been no changes in price of the comparators.

In TA404, the committee preferred to assume no overall survival benefit for degarelix compared with LHRH agonists and no difference in the rate of fractures and cardiovascular events and this had a large impact on the cost-effectiveness results. Given the uncertainty in these areas, the committee’s preferred assumptions were conservative, and no new relevant clinical effectiveness evidence has been identified from the literature searches.

Overall, no new evidence has been identified that is likely to change the existing recommendations in TA404 therefore it is proposed this guidance should be transferred to the ‘static guidance list’.

Summary of new evidence and implications for review

Has there been any change to the price of the technology(ies) since the guidance was published?

The company has confirmed that the discount for degarelix is still in place and is unchanged from 2016. There have been no changes in the prices of the comparators (leuprorelin, goserelin and triptorelin) since TA404 was published.

Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?

None

Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?

In TA404, the committee preferred to assume no overall survival benefit for degarelix compared with LHRH agonists and no difference in the rate of fractures and cardiovascular events and this had a large impact on the cost-effectiveness results. No new evidence from relevant randomised controlled trials comparing degarelix with LHRH agonists was identified. Several meta-analyses have been published since TA404 but these generally included trials that had already been considered during the development of the appraisal. Furthermore, the committee's preferred assumptions were conservative, therefore any new trials showing a survival benefit for degarelix is unlikely to change the existing positive recommendation for people with spinal metastases.

All ICERs for the full population were above the range normally considered a cost-effective use of NHS resources. The PRONOUCE trial compares degarelix with leuprolide and is currently on-going (results due 2021). PRONOUNCE examines the risk of cardiovascular complications in patients with advanced prostate cancer and cardiovascular disease. This trial only covers a subgroup of the population in the full marketing authorisation therefore any clinical effectiveness evidence is unlikely to change the existing negative recommendation for the full population. No new trial evidence comparing degarelix with LHRH agonists in the full population has been identified.

Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?

NG131 Prostate cancer: diagnosis and management has been updated and was published in 2019 but does not cover the use of degarelix.

Additional comments

The search strategy from the original ERG report was adapted for the Cochrane Library, Medline, Medline In-Process and Embase. References from March 2013 to August 2020 were reviewed. Additional searches of clinical trials registries and other

sources were also carried out. The results of the literature search are discussed in the ‘Summary of evidence and implications for review’ section above. See Appendix C for further details of ongoing and unpublished studies.

Equality issues

During scoping, consultees raised a potential equality issue relating to prostate cancer being more common amongst older men and men who are African Caribbean. However, the recommendations in TA404 did not have an adverse impact on people with these characteristics and therefore the committee concluded that no relevant equalities issues were identified during the development of the appraisal.

Proposal paper sign off

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Appendix A – Information from existing guidance

Original remit

To appraise the clinical and cost effectiveness of degarelix within its licensed indication for the treatment of advanced hormone-dependent prostate cancer.

Current guidance

1.1 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.

1.2 This guidance is not intended to affect the position of patients whose treatment with degarelix was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

Research recommendations from original guidance

Further research is recommended to resolve uncertainties about the clinical effectiveness of degarelix compared with LHRH agonists such as leuprorelin, goserelin and triptorelin for treating advanced hormone-dependent prostate cancer, particularly in subgroups of people with pre-existing cardiovascular disease, people with skeletal (including spinal) metastases and people with impending ureteric and urethral obstruction. Research should be planned as part of well-conducted randomised clinical trials.

Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the STA process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred	NICE will reconsider whether a review is necessary at the specified date.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No
The guidance should be updated in an on-going clinical guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

Options	Consequence	Selected – 'Yes/No'
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider.	Yes
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

Appendix C – Other relevant information

Relevant Institute work

Published

Prostate cancer: diagnosis and management (2019) NICE guideline 131

Prostate cancer (updated 2019) NICE pathway

In progress

Nothing relevant (19/08/20)

Details of changes to the marketing authorisation for the technology

Marketing authorisation and price considered in original appraisal

Degarelix has a marketing authorisation in the UK for the 'treatment of adult male patients with advanced hormone-dependent prostate cancer'.

The cost of 2×120-mg vials is £260.00 and an 80-mg vial is £129.37 (excluding VAT; British national formulary May 2015). The company has agreed a nationally available price reduction for degarelix with the Commercial Medicines Unit. The company also has a commercial scheme available to clinical commissioning groups. The reduced prices are commercial in confidence.

Proposed marketing authorisation (for this appraisal) and current price

No planned changes to the marketing authorisation.

The cost of 2×120-mg vials is £260.00 and an 80-mg vial is £129.37 (BNF 02 July 2020) is unchanged. The price reduction remains unchanged.

Registered and unpublished trials

Trial name and registration number	Details
An Open-label, Single-Arm, Multicenter, Phase IV Trial to Evaluate the Safety of Firmagon® in Androgen Deprivation Therapy in Indian Patients Diagnosed With Advanced Hormone-dependent Prostate Cancer (NCT02726009)	Phase IV interventional study 228 participants Active, not recruiting Estimated Study Completion Date: December 2020

Trial name and registration number	Details
A Multi-Center, Randomized, Assessor-Blind, Controlled Trial Comparing the Occurrence of Major Adverse Cardiovascular Events (MACEs) in Patients With Prostate Cancer and Cardiovascular Disease Receiving Degarelix (Gonadotropin-Releasing Hormone (GnRH) Receptor Antagonist) or Leuprolide (GnRH Receptor Agonist) (NCT02663908)	Phase III interventional study 900 participants Recruiting Estimated Study Completion Date: July 2021
A Phase 3 Study of Androgen Annihilation in High-Risk Biochemically Relapsed Prostate Cancer (NCT03009981)	Phase III interventional study 504 participants Recruiting Estimated Study Completion Date: January 2023
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 (NCT02799706)	Phase III interventional study 885 participants Recruiting Estimated Study Completion Date: June 2024