17 January 2018

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Dear Colleague

**Abiraterone in newly diagnosed hormone naive prostate cancer**

Abiraterone is currently licensed and accepted by SMC for the treatment of prostate cancer once resistance to standard hormone therapy has developed.

In 2017 two large phase 3 randomised clinical trials were published, one academic and one commercial registration, which evaluate the benefit of adding abiraterone to androgen deprivation therapy (ADT) in newly diagnosed hormone naive prostate cancer. The publication of these trials presented two key challenges for NHS Scotland medicines governance and technology assessment processes:

- It is rare for such a robust evidence base for the off label use of a medicine to be in the public domain so far ahead of license and SMC consideration.
- The eligible population in the two trials were different:
  - The commercial registration trial included only high risk metastatic prostate cancer patients.
  - The academic trial included a broader population of both metastatic (low and high risk) and locally advanced prostate cancer. As use in low risk metastatic and locally advanced disease was not included in the commercial trial, this is ‘off-label’ and outwith the scope of SMC.

NHS Boards reported that requests for early access to this medicine for individual patients, through unlicensed medicines processes, were being considered and sought advice from Healthcare Improvement Scotland (HIS).

**Method**

Work is underway within HIS to develop guiding principles and an operational framework to improve consistency in the assessment of evidence and development of guidelines for off-label use of cancer medicines. As the Chair and National Clinical Lead for the Off Label Cancer Medicines Short Life Working Group (SLWG) we were asked to facilitate a meeting of key stakeholders to gain a consensus to support an equitable response to this evidence across NHS Scotland. A meeting of key stakeholders including the cancer networks, Directors of Pharmacy, SMC and public partners was convened in November 2017 to consider the available evidence.

The purpose of the meeting was to form a consistent and equitable response to this evidence across NHS Scotland until marketing authorisation (MA) is approved and SMC advice is available for the
licensed indication. Additionally, the group were to consider how NHS Scotland should address the evidence for off-label use (i.e. not covered by the new licensed indication).

Soon after the meeting the EMA granted marketing authorisation for the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer. Assuming a timely submission is received from the company, SMC advice in line with the MA, on the medicine is expected in August 2018.

The group considered the available evidence on clinical effectiveness, budget and service impact alongside evidence in practice from clinicians present. There was no health economic evidence available to the group. It is understood that an academic economic analysis of the academic study is underway however this is not expected to be available before spring 2018.

Conclusion

The SLWG found that the evidence base to be insufficient to provide interim guidance. Until SMC advice and national guidance on the off label use is available, access to abiraterone in this indication should remain subject to Peer Approved Clinical System (PACS) Tier 2\(^3\) (for the licensed indication) or individual off label request process (off label use). While each case will be subject to individual local review the group recommends that only cases of high risk and low risk metastatic prostate cancer where there is an absolute contraindication to docetaxel should be considered. Uro-oncologists have advised that this represents a small proportion of the eligible population and may be in the region of 50 patients per annum across Scotland.

Key points for NHS Boards and the advice above to support the review of individual requests is outlined in the attached appendix alongside a recommendation on the way forward for the review of the ‘off label’ indication.

Please contact Mary Maclean mary.maclean4@nhs.net if you have any queries on this advice.

Yours sincerely

Professor David Cameron  
Chair – Abiraterone Stakeholder Group Meeting  
On behalf of the Healthcare Improvement Scotland Medicines Team

Mary Maclean  
National Clinical Lead – Cancer Medicines

References:


3. PACS Tier 2: Peer Approved Clinical System Tier 2 is replacing the existing Individual Patient Treatment Request (IPTR) system
Appendix: Abiraterone in newly diagnosed hormone naive prostate cancer

A. Key points for NHS Boards

- Two large phase 3 randomised clinical trials, one academic[1] and one commercial registration[2], demonstrate a survival benefit when abiraterone is added to androgen deprivation therapy (ADT) in newly diagnosed hormone naive prostate cancer.
- An independent critical evaluation of the two studies demonstrated both trials were of high quality and are relevant to patients in Scotland.
- Health economic evidence is required in order to make a full assessment in line with NHS Scotland process for evaluating new medicines.
- It would not be appropriate for the group to pre-empt SMC advice.
- There is insufficient evidence at this time to support consideration in locally advanced prostate cancer.
- The current standard of care for newly diagnosed hormone naïve metastatic prostate cancer is docetaxel in combination with androgen deprivation therapy. This indication is ‘off label’.
- There is no evidence currently that abiraterone is better than docetaxel in terms of overall survival benefit in this setting.
- Although docetaxel is an alternative which provides similar benefit, there is a significant proportion of patients who are unfit for docetaxel.
- Until SMC advice and national guidance on the off label use is available, access to abiraterone in this indication should remain subject to PACS Tier 2[3] (for the licensed indication) or individual off label request process (off label use).

B. Advice to support the review of individual requests for treatment

While each case will be subject to individual local review the SLWG recommends that only cases of high risk and low risk metastatic prostate cancer where there is an absolute contraindication to docetaxel should be considered. Uro-oncologists have advised that this represents a small proportion of the eligible population and may be in the region of 50 patients per annum across Scotland.

C. NHS Scotland review of the ‘off label’ indication

- As the results from both trials are very similar in terms of overall survival and progression free survival benefit it is difficult to justify limiting access to the cohort of patients under licensed indication.
- Therefore a concurrent review of the ‘off-label’ indication should be done in parallel with SMC review of the licensed indication.
- It is not within the remit of SMC to assess ‘off-label’ medicine use so this will be led by the HIS Medicines Team aligning it with the evolving national process for review of off-label cancer medicines.


3. PACS Tier 2: Peer Approved Clinical System Tier 2 is replacing the existing Individual Patient Treatment Request (IPTR) system