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Because health matters

27th January 2006

Ms. Alana Miller
Technology Appraisal Project Manager
National Institute for Health and Clinical Excellence
Mid City Place
71 High Holborn
London WC1V 6NA

Dear Ms. Miller,

RE: ACD – docetaxel for the treatment of hormone-refractory metastatic prostate cancer.

We welcome this opportunity to review and comment on the Appraisal Consultation Document (ACD) on docetaxel for the treatment of hormone-refractory metastatic prostate cancer (mHRPC). We believe that all the relevant evidence has been taken into account, and that the summaries of clinical effectiveness are reasonable interpretations of the available evidence with the following caveats:

Appraisal Committee's preliminary recommendations: Section 1.3

The ACD discusses when repeat cycles of docetaxel may not be recommended including following relapse after initial successful response. Clarification on the definition of relapse may be required, as there may be confusion. It is not uncommon for patients to have intermittent chemotherapy breaks, which are not due to relapse. Therefore disease progression relapse is distinct from a treatment break.

Clinical Need and Practice: Section 2.11

The ACD implies that the British Association of Urological Surgeons (BAUS) guidelines for second-line treatment of hormone-resistant disease recommend use in just asymptomatic patients; however, their recommendation actually includes all "fit"patients. The BAUS guidelines, therefore, state "Docetaxel improves pain, patient quality of life, and overall survival and should be considered in all patients with mHRPC who are sufficiently fit for chemotherapy".[1] This is an important clarification as "fit" patients will be defined regardless of whether they are symptomatic or asymptomatic.

The recent MDT (Multi-disciplinary Team) Guidance for Managing Prostate Cancer Produced by BAUS, British Uro-oncology Group (BUG) and British Prostate Group (BPG)[2] also recommends chemotherapy in patients who are metastatic and hormone-refractory. Stating "Those who do not respond to maximal second-line hormonal therapy are considered to have hormone-refractory disease and are candidates for chemotherapy, novel therapies and/or symptomatic local treatments".

In addition, the European Association of Urology[3] guidelines also support the use in *all* mHRPC patients, specifically recommending docetaxel use in patients with mHRPC as being the reference treatment.

Consideration of the evidence:

Section 4.3.4

The ACD reviews both the TAX-327 study and a pooled meta-analysis in their review of docetaxel. In order to avoid potential confusion we would suggest clarifying that the Quality of Life (QoL) conclusion covered in Section 4.3.4 is highlighted as referenced to the pooled meta-analysis i.e.:
"there was insufficient evidence *at present based on the pooled metanalysis* to support the assertion that docetaxel provides benefits in quality of life and palliation over and above those associated with the use of mitoxantrone". However, in the randomised study TAX-327, docetaxel has shown significant QoL benefits in terms of pain response and prostate-specific symptoms, compared to mitoxantrone. This benefit has been recognised in section 4.1.5.

Section 4.3.5

We agree with the comments made in Section 4.3.5. We would like to highlight that most centres will have a pro-active side-effect management protocol; and either prophylactically prevent side effects occurring with docetaxel in prostate cancer, or pro-actively brief patients on what can be expected, giving docetaxel a manageable and predictable side effect profile in Prostate Cancer.

Section 4.3.6

We are pleased that the committee accepted the extrapolation of clinical data beyond the trial period, and find both the manufacturer and assessment group models acceptable.

Proposed recommendations for further research: Section 5.1

The MRC Study (STAMPEDE) and other trials such as TRAPEZE review docetaxel in combination with bisphosphonates and radio-isotopes, These studies incorporate quality of life (QOL) assessments and have study populations in line with, and representative of, the wider patient population in terms of age, performance status and co-morbidity, and will therefore, serve to enhance the volume of information available for this product in this licence indication for the future.

To conclude, we consider that the provisional recommendations of the Appraisal Committee, in line with the additional comments suggested, are sound and constitute a suitable basis for the preparation of guidance to the NHS.

Yours sincerely

Mike Baldwin
Head of Health Technology Appraisals

References:

1. Second-line systemic treatment of hormone-resistant disease. Guidelines on Treatment. British Association of Urological Surgeons. June 2005.
2. MDT (Multi-disciplinary Team) Guidance for Managing Prostate Cancer. British Association of Urological Surgeons (BAUS) Section of Oncology; British Uro-oncology Group (BUG); British Prostate Group (BPG). 2005
3. AUS G, et al. EAU Guidelines on Prostate Cancer. European Urology 2005 (48): 546-551