27th October 2005

Ms. Alana Miller
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71 High Holborn
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Dear Alana,

RE: Docetaxel for the treatment of hormone refractory prostate cancer – Assessment report

On behalf of sanofi-aventis we would like to thank you for providing us the Assessment Report which details a systematic review undertaken to evaluate the clinical and cost-effectiveness of docetaxel in combination with prednisone /prednisolone for the treatment of metastatic hormone refractory prostate cancer (mHRPC).

We welcome the overall conclusions of the report which we believe is a fair and balanced assessment of the evidence available.

The assessment of clinical effectiveness of docetaxel (versus other treatments), is factually correct, and represents a reasonable interpretation of all the relevant evidence that needs to be taken into consideration.

The two randomized controlled phase III trials detailed in the report, the TAX 327 and SWOG 9916, have demonstrated that docetaxel-based treatments are the most effective regimens that have emerged thus far in mHRPC offering significantly more effective palliation and improved survival, than mitoxantrone-based therapy. We also accept that although there is little evidence comparing docetaxel plus prednisone to steroids alone in a randomised setting, the indirect comparisons do support the widely accepted view that docetaxel plus prednisolone is superior to corticosteroids alone in terms of overall survival and palliation.

We know that patients with mHRPC have an extremely poor prognosis, and many who receive best supportive care alone, could expect a median survival period of between 9 and 12 months[1,2], whilst those who receive mitoxantrone plus steroid therapy, could expect at best, a median survival of between 12 and 15 months[3,4]. The results from TAX 327 and SWOG 9916 demonstrated that chemotherapy could significantly advance the survival duration yet further. The median survival of 18.9 months (95% CI: 17.0-21.2) reported in TAX327, represents a significant milestone for those who are approaching the end stage of their disease and for whom there is a clear unmet medical need for active and effective

palliative treatment that can bridge the gap between the failure of hormonal therapy and the initiation of terminal stage palliative care. The review of the clinical data suggests that docetaxel plus prednisone is the most effective treatment to do this.

Increasingly, this view has been supported by independent bodies. The findings from TAX327 and SWOG 9916, have been instrumental in the wider acceptance of the role of chemotherapy, in the treatment of mHRPC. Guidelines drawn up by the BAUS (British Association of Urological Surgeons) specifically recommend that patients with symptomatic mHRPC who are fit for chemotherapy should be considered for therapy with docetaxel. In addition, the London Cancer New Drugs Group which represents six cancer networks in London and Hertfordshire, has recognised that 'given the strength of the evidence, the use of docetaxel in patients with mHRPC should be supported'[5].

We support the conclusion of the economic evaluation conducted by the Assessment Group that docetaxel (3-weekly) plus prednisone/prednisolone is cost-effective, provided the NHS is willing to pay £32, 706 per QALY. The general robustness of this figure was also demonstrated with a range of sensitivity analysis. We also agree with the Assessment Group that this figure should be considered as conservative as it does not include any additional palliative benefits conferred by any of the chemotherapy regimens.

In summary, we support the overall recommendation made, based on the review of clinical and economic evidence submitted and the evidence available.

Yours sincerely

Mike Baldwin

Head of Health Technology Appraisals

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References

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3. Kantoff P.W., Halabi S., et al. (1999) Hydrocortisone with or without mitoxantrone in men with hormone-refractory prostate cancer: results of the cancer and leukemia group B 9182 study. *J Clin Oncol*, 17, 25

4. Samelis G.F., et al. (2003) The combination of estramustine and mitoxantrone in hormone-refractory prostate cancer: a phase II feasibility study conducted by the Hellenic Cooperative Oncology Group. *Urology*, 61, 121

5. London-Cancer-New-Drugs-Group (2005) http://www.druginfozone.nhs.uk/.