The Department of Health

Comments on Appraisal Consultation Document relating to:
Pemetrexed for the treatment of non-small cell lung cancer

General comments

Around 35% of patients with NSCLC in the UK receive 1st Line chemotherapy. The proportion of those who go on to receive second line chemotherapy is not well researched but, based on experience, our clinical colleagues would estimate that not more than 20% of this 35% go on to receive 2nd line chemotherapy (i.e. 7% overall). This very low proportion is largely a result of the fact that many oncologists feel the toxicity and overall poor tolerability of docetaxel in this group of patients at this stage of their disease is too high to outweigh the relatively low response rates and modest survival gain. There is a very high rate of hospitalisation for febrile neutropaenia with docetaxel (well over 10% in our experience) and alopecia is common. Good, less toxic agents are urgently required in this setting. Having less toxic alternatives available would result in a higher proportion of patients receiving second line therapy which clinical colleagues feel would be likely to result in a modest, but significant improvement in survival and quality of life in this particular group of patients for whom there are currently limited options.

Apart from the generality of patients potentially eligible for second line chemotherapy, clinical colleagues advise that there are at least two specific sub-groups of patients in whom the availability of an effective alternative to docetaxel as second line treatment is *urgently required*; these are:

- Patients allergic to Docetaxol
- Patients who received Docetaxol first line and who have relapsed

There is also a larger group of patients who are currently considered unfit for docetaxel who could benefit from a less toxic agent.

We would be grateful if NICE could reconsider the limited options available to patients and oncologists in this common clinical situation and the potential benefits to survival (if modest), quality of life and lower toxicity profile of Pemetrexed. Alternatives to docetaxel are urgently needed for a limited number of patients.

Specific comments on appraisal

In our opinion, we feel the guidance may have mis-judged the significance of the differences of the toxicity profiles of docetaxel vs. pemetrexed, particularly as they affect this specific patient group. We also feel the guidance may have underestimated the costs of the growth factor support (GSF) with docetaxel by possibly underestimating the proportion of patients who should be receiving it - treatment which ASCO guidelines recommend routinely in the management of febrile neutropaenia and even prophylactically in patient groups with a high likelihood of this adverse event. We feel that the lower requirement for the use of GSF with pemetrexed alone would make a significant impact on the ICER.

The guidance does not make it clear how the ERG arrived at some of their cost estimates, especially the cost per QALY of £458,333 – would it be possible to set out these analyses more clearly?

In addition, the ERG used an average Body Surface Area of 1.83m^2 to calculate the average cost of a course of pemetrexed treatment – in the experience of clinical colleagues, this is significantly higher than patients in this disease group in the UK. They estimate it to be between 1.65 and 1.7 – a difference that would significantly reduce the cost per QALY of pemetrexed.