Pemetrexed for the Treatment of Non-Small-Cell Lung Cancer

Response to the Appraisal Consultation Document from the National Institute for Health and Clinical Excellence.
October 2006

Comments submitted on behalf of the Royal College of Physicians, the Royal College of Radiologists, the Association of Cancer Physicians, the Joint Collegiate Council for Oncology, and the National Cancer Research Institute Lung Cancer Group

- Around 35% of patients with NSCLC in the UK currently receive 1st Line chemotherapy.
- The proportion of these who go on to receive second line chemotherapy is not well researched but expert opinion from the National Lead Clinician for lung cancer and from the National Lung Cancer Audit programme suggests that no 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 most centres) and alopecia is common – another very distressing side effect for patients with only a few months to live.
- Good, less toxic agents are urgently required in this setting. Having less toxic alternatives available would result in a higher proportion of patients being eligible to receive second line therapy which 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.
- Pemetrexed is such an alternative and as such needs serious consideration.
- We believe that NICE has failed to recognise the significance of the differences of the toxicity profiles of docetaxel in comparison with pemetrexed, particularly as they affect this specific patient group. We also believe that NICE have underestimated the costs of the growth factor support (G-CSF) required for the safe administration of docetaxel by underestimating the proportion of patients who should be receiving it. ASCO guidelines recommend the routine use of G-CSF in the management of patients with febrile neutropenia and also recommend the prophylactic use of G-CSF in patient groups with a high likelihood of this adverse event.

- Pemetrexed has substantially less haematological toxicity than docetaxel and therefore G-CSF would be rarely required. We believe that this lower requirement for the use of G-CSF should significantly reduce the ICER for pemetrexed in comparison with docetaxel
- It is not clear to us how the ERG arrived at some of their cost estimates, especially the cost per QALY of £458,333 – it is vital that these crucial analyses are entirely transparent and consistent. We are not convinced that the analyses of the ERG meet either of these requirements.
- We would also like to point out that the ERG used an average Body Surface Area of 1.83m^2 to calculate the average cost of a course of pemetrexed treatment - this in our experience is significantly higher than patients in this disease group in the UK. We estimate it to be between 1.65 and 1.7 – a difference that would significantly reduce the ICER for pemetrexed.
- Apart from the generality of patients potentially eligible for second line chemotherapy, 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 docetaxel
      Patients who received docetaxel first line and who have relapsed
- There is also a larger group of patients, as implied in the opening paragraph, who are currently considered unfit for docetaxel who could benefit from a less toxic agent.
- We would therefore urge NICE to 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. We urgently need alternatives to docetaxel for a limited number of patients.