Dr. Carole Longson
Director
Centre for Health Technology Evaluation
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Dear Dr. Longson,

Thank you for the opportunity to comment on the Appraisal Consultation Document for pemetrexed disodium for the treatment of meothelioma. I send these comments on behalf of the British Mesothelioma Interest Group (Consultee) and the British Thoracic Oncology Group (Commentator).

We are very disappointed with the ACD that rules that pemetrexed disodium is not recommended for the treatment of malignant pleural mesothelioma.

From a clinical standpoint, the recruitment of approximately 450 patients with a rare tumour into an International Phase III Clinical Trial over such a short period of time is to be applauded. The trial demonstrated a statistically significant benefit for the use of pemetrexed in combination with cisplatin, compared with cisplatin alone. Pemetrexed is now the only licensed treatment for mesothelioma, a fatal malignancy inevitably caused by asbestos exposure. The use of cisplatin as a control arm has been criticised. Whilst this is not a commonly used single agent for the treatment of mesothelioma in the England and Wales, it is commonly combined with other agents at the current time for patients with this disease, most notably mitomycin and vinblastine (MVP). Indeed, a metaanalysis (Berghmans, 2002) suggested that cisplatin was the most active drug for mesothelioma so this is not an inappropriate control treatment for the Phase III trial.

There are no randomised trials that have been published that compare chemotherapy with active symptom control – this is being investigated in the MSO-1 trial. However, the chemotherapy regimens used in this trial (either MVP or vinorelbine) were based on very small Phase II clinical trials. Therefore, the result of this trial is not going to help shed light on whether chemotherapy is superior to active symptom control.

The incidence of mesothelioma in the UK is likely to increase over the next 5-10 years, after which it is likely to decline significantly. It is imperative that this is considered – this is not a malignancy that is likely to have a huge impact on the resources of the NHS for years to come.

Much is said about recruitment into clinical trials and, as Oncologists, we are continually encouraged (rightly) to enrol patients into appropriate clinical trials. Despite many centres around the World recruiting into the Phase III trial, it is hugely frustrating that the result, a significant one, is going to have no effect on the clinical practice of a hugely distressing disease.

The Appraisal Document identifies a need for randomised controlled trials comparing alternative treatment regimens in MPM – this has been done (see above) and the results will have no impact on clinical practice. The Committee recommends that trials be conducted in which pemetrexed is compared with treatments currently commonly used in England and Wales (notably MVP, vinorelbine and active symptom control) in order to determine its relative effectiveness. Pemetrexed has been tested in combination with cisplatin versus cisplatin alone (the likely most active drug of the MVP combination). It is difficult to justify a clinical trial that would use the only licensed drug in mesothelioma and compare this with active symptom control – recruitment would be near impossible. The time taken to conduct these trials would mean this is a huge backward step for the treatment of this disease. The Committee also suggests that comparative trials of pemetrexed versus other promising agents be conducted – whilst this is a reasonable suggestion it is hard to see how this will be possible if pemetrexed is not allowed to be routinely prescribed.

In addition, we feel the cost effectiveness data are incredibly complex and we are not sure exactly how reliable these are.

In summary, we feel the guidance is hugely disappointing for mesothelioma sufferers and the Oncologists and other members of the healthcare profession who work so tirelessly to improve the lives of this unfortunate group of patients.

Yours sincerely

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Comments on behalf of:
British Mesothelioma Interest Group (Consultee)
British Thoracic Oncology Group (Commentator)