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Chris Feinmann
Project Manager Single Technology Appraisals
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25 October 2007

Dear Mr Feinmann

Re: Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma (review of technology appraisal guidance 37) - Appraisal consultation document

I write on behalf of the NCRI Lymphoma Clinical Studies Group, the Royal College of Physicians, the Royal College of Radiologists, the Joint Collegiate Council for Oncology and the Association of Cancer Physicians in response to the Appraisal Consultation Document for the above technology. We are grateful for the opportunity to review this and would like to make the following comments:

1. We welcome the review and agree that the relevant evidence of clinical benefit has been considered.
2. We agree that the review of guidance 37 relating to use of Rituximab as a single agent in second or subsequent relapse has reached the appropriate conclusion, as expressed in recommendation 1.1.
3. We also agree with the recommendation that Rituximab be available as maintenance therapy following successful treatment of recurrence with chemotherapy, but would also recommend maintenance Rituximab be given after treatment with chemotherapy-Rituximab in combination.
4. We do not concur with the view that chemotherapy alone (without Rituximab) should be recommended for the treatment of recurrent follicular lymphoma, as put forward in recommendation 1.3. This conclusion is not sound and would not constitute a suitable basis for preparation of guidance to the NHS.

We were not persuaded by the ERG calculation of cost per QALY decreasing the duration of treatment benefit to 2 years. No logical argument was advanced for this limitation of benefit which appears to artificially inflate the cost. An equally good clinical argument could be made for a benefit horizon of 3, 5 or 10 years.

The assertion that Rituximab will be generally given as day-case rather than out-patient therapy owing to the duration of infusion (para 3.9) is incorrect. The practice of rapid (90 minute) administration is now widespread following description of its safety in the literature (Sehn et al., Blood. 2007 May 15;109(10):4171-3).

The most important consideration in denying patients access to chemotherapy-Rituximab combination for re-induction of remission is that the response rate has been consistently shown to be lower for chemotherapy alone. Since patients will only receive maintenance therapy if they have shown a response to re-induction therapy, the lower response rate would deny a significant proportion of patients access to maintenance therapy, which the appraisal committee has already indicated should be made available.

The net effect would be to contradict the committee's own recommendation in 13%-24% of patients: this is the difference in response rates with or without Rituximab in the EORTC and German Low Grade Lymphoma Study Group trials respectively. It is therefore the proportion of patients who would go on to receive maintenance Rituximab after Rituximab-chemotherapy, but not after chemotherapy alone. It would be perverse to recommend a treatment, and simultaneously make a recommendation which would deny that treatment to around 20% of those who would benefit from it.

I trust these comments will be of use.

Yours sincerely