csas
Commissioning Support
Appraisals Service

NHS

[redacted]

24 November 2011

National Institute for Health and Clinical Excellence

Dear [redacted]

RE: Rituximab in combination with chemotherapy for treatment of symptomatic stage III and IV follicular lymphoma

On behalf of Commissioning Support, Appraisals Service (CSAS), Solutions for Public Health, I would like to submit our comments on the appraisal consultation document for ***Rituximab in combination with chemotherapy for treatment of symptomatic stage III and IV follicular lymphoma***.

In general, CSAS supports NICE's provisional recommendation that "Rituximab, in combination with cyclophosphamide, vincristine and prednisolone (CVP), cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP), mitoxantrone, chlorambucil and prednisolone (MCP), or cyclophosphamide, doxorubicin, etoposide, prednisolone and interferon-α (CHVPi), is recommended as an option for the treatment of symptomatic stage III and IV follicular lymphoma in previously untreated people".

Rituximab in combination with chemotherapy is more clinically effective than chemotherapy alone. There is evidence to demonstrate that Rituximab plus CVP, CHOP, MCP and CHVPi is more effective than CVP, CHOP, MCP and CHVPi alone for the treatment of advanced follicular lymphoma. The addition of rituximab to CVP, CHO and MCP produced statistically significantly improved rates of overall survival at 4 or 5 years. The addition of rituximab to CVP, CHOP, MCP and CHVPi improved progression-free survival and duration of response.

Rituximab in combination with specified combination chemotherapy regimens does appear to be a cost effective use of NHS resources. NICE considered cost-effectiveness analyses, with or without the addition of rituximab, for the chemotherapy regimens CVP, CHOP and MCP and considered the manufacturer's submission for CHVPi. The addition of rituximab to CVP, CHOP, MCP and CHVPi gave incremental cost-effectiveness ratios (ICERs) of: £7720, £10,800, £9320 and £9251 respectively per QALY gained, and these are well below NICE's usual ceiling of £20,000-£30,000/QALY.

No issues with safety were raised. The addition of rituximab to CVP, CHOP, MCP and CHVPi did not significantly increase adverse event rates.

The quality of available research was good. The assessment of efficacy was based on four good quality trials, which included chemotherapy regimens used in the NHS (CVP, CHOP, MCP and CHVPi). It would not be appropriate to generalise these results to other chemotherapy regimens, for example, those containing chlorambucil, fludarabine or bendamustine.

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There were, however, limitations to the inputs in the economic model. Neither the manufacturer nor the Assessment Group models included the use of rituximab as maintenance treatment after induction therapy, or modelled the re-use of rituximab as second-line treatment where it may be less effective. It was probably reasonable for the Appraisal Committee to consider that there was insufficient uncertainty to increase the ICER above £20,000-30,000/QALY. It should be noted that the ICER estimates for R-CHVPi were taken solely from the manufacturer's submission, but the Assessment Group was probably reasonable in not including this chemotherapy combination in its model due to design issues with the trial and because the combination is infrequently used in clinical practice

Crude cost estimates suggest that the addition of rituximab to CVP, CHOP, MCP and CHVPi would cost an additional £20,000 per 100,000 population per year (i.e. to treat two patients per 100,000 population per year) in drug costs alone. The impact of VAT and locally negotiated prices could make an important difference to the true cost to commissioners.

If you require any further information please contact me directly: [redacted]

Yours sincerely

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