Comments on the ACD Received from the Public through the NICE Website

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	I am a member of the Commissioning Support appraisal Service National Steering Group
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The provisional recommendations extend the use of rituximab in patients with follicular non-Hodgkin's lymphoma as maintenance treatment following first line chemotherapy. After review of the manufacturer's evidence submission and cost-effectiveness modelling, NICE recommends rituximab as an option for maintenance treatment in patients with advanced follicular non-Hodgkin's lymphoma that has responded to first-line induction therapy with rituximab in combination with chemotherapy. This must be considered in the context of failure to demonstrate improvements in overall survival, and uncertainties about the use of salvage chemotherapy following disease progression. The manufacturer's model was based over a 6 year time period, despite only 4 years' follow up in the PRIMA study.
Section 2 (The technology)	The provisional recommendations could increase the use and therefore the overall cost of this drug for a PCT population. According to the manufacturer's estimates, the cost of treating a person with an average body surface area of 1.8m2 with rituximab maintenance treatment for 2 years is £14,669. Implementing this guidance could carry additional annual drug costs of approximately £380,000 for the average PCT of 300,000 people with an estimated 52 people receiving maintenance treated with rituximab for this indication per year.
Section 3 (The manufacturer's submission)	Substantial amounts of data have been redacted in this ERG report. The most relevant RCT is a phase III study called the PRIMA trial and this forms the basis of the manufacturer's submission. Data from the post-study observational follow-up period, which had a median follow-up of 38 months, were submitted to the ERG as 'academic in confidence' and will become more generally available when and if they are published. We note that the ERG cautioned that the data were immature and that the early closure of the trial might have led to an overestimation of the clinical benefits of rituximab maintenance treatment.
Section 4 (Consideration of the evidence)	The PRIMA study Longer-term data are not available from the PRIMA trial so the manufacturer modelled the expected survival outcomes using data from a separate study - the EORTC 20981 study (a phase III, open-label randomised trial that included 465 people with relapsed or resistant follicular non-Hodgkin's lymphoma who had not previously been treated with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) or R-CHOP, who were randomised to induction with CHOP or R-CHOP then randomised between maintenance rituximab or

	observation until relapse), which was also used to help estimate the transition probabilities between health states and death in the economic model. It is important to note that study evidence did not show a statistically significant improvement in survival after 5 years in EORTC 20981. In the manufacturer's base case analysis, rituximab maintenance was cost effective compared with observation when the benefits of rituximab are assumed to last for 6 years (ICER £15,978/QALY). In sensitivity analyses undertaken by the ERG, ICERs ranged from £21,000 to £26,000 per QALY when the benefit was assumed to be sustained for the first 3 to 4 years.
Section 5 (Implementation)	
Section 6 (Related NICE guidance)	The ERG agreed to the manufacturer's small changes to the decision problem, i.e. by considering the treatment in people who had responded to first-line treatment with rituximab plus chemotherapy rather than as specified in 'adults with advanced follicular lymphoma that has responded to first-line chemotherapy'. There are two effects of this. One of the comparators that was originally specified in the scope, ibritumomab tiuxetan, has been excluded from analysis. The determination has also pre-empted the findings of the review of TA 110 'Rituximab for the first-line treatment of stage III-IV follicular lymphoma' which will report in 2011 and considers a wider range of rituximab containing regimens for first induction.
Section 7 (Proposed date of review of guidance)	
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