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| <b>NICE Health Technology Appraisal - Assessment Report<br/>On</b> |   |
| <b>RITUXIMAB FOR FOLLICULAR LYMPHOMA (REVIEW OF TA110)</b>         |   |
| <b>TO: NICE</b>  | <b>FROM: Healthcare Improvement<br/>Scotland 13 June 2011</b> |

1. Comment provided to Healthcare Improvement Scotland by: Dr Anne Parker MD FRCP FRCPath, Consultant Haematologist

My comments are as follows

The document gives a good account of the current management for stage III/IV follicular NHL in England and Wales which is comparable with management in Scotland.

There is one glaring error on page 14 in the description of systemic symptoms where I think there has been a transposition it should read A absence and B presence of systemic symptoms rather than as described.

The limitations due to lack of data are well described in this data and confounding features of multiple lines of therapy in a disease with a relatively long overall survival well documented.

I think the AG have come up with a reasonable model for the majority of patients in terms of disease outcomes and the data that is being fed into it. I am not competent to comment on the statistical methods they have used to derive their final figures.

This seems very brief after a 300 plus page document but essentially I think it is a reasonable assessment of a very complex subject

2. Comment provided to Healthcare Improvement Scotland by: Dr Dominic Culligan Consultant Haematologist

I have read this most detailed NICE Appraisal Report into the use of Rituximab coupled with chemotherapy in the treatment of follicular lymphoma. The report does not specifically address the role of Rituximab maintenance but does incorporate first line maintenance in the economic modelling. Clearly the report is very thorough and I have little if any criticism of the technical aspects of the report.

From the point of view of clinical effectiveness the review group have identified the four randomised controlled trials and I am not aware of additional appropriate trial data that has been overlooked. The clinical effectiveness conclusions seem correct and in keeping with the real life perceived clinical benefit of R-Chemotherapy (predominantly R-CVP and R-CHOP) as used in routine clinical practice in the UK including Scotland for several years now.

From the point of view of the in-house economic modelling I believe the treatment algorithms to be broadly representative of clinical practice. There will always be some discussion of the position of transplantation and there has been a tendency to move from second line transplantation to third line because of the availability and use of Rituximab maintenance in second remission. With the recent SMC approval of Rituximab maintenance in first remission there may now be a subsequent move back to considering transplant in second remission, especially in patients who relapse on or soon (< 12 months) after Rituximab maintenance. A further issue with transplantation is an increasing use of reduced intensity conditioned allografting in second remission for poor risk patients (e.g. relapse < 12 months from R-CHOP) rather than the traditional autograft which is modelled. Whilst overall such numbers are still small the additional costs might have an increasing impact on the model.

The Review Group have identified many of the uncertainties and applied a wide range of sensitivity analyses. I agree that the crucial questions in clinical practice are the subsequent benefit of R-chemotherapy in second line when R-chemotherapy was used in first line. This is even more unclear when you take into account routine R-maintenance in first line. The role of R-maintenance in second line is even more unclear following R-maintenance in first line.

Overall the conclusions on clinical benefits seem sound and the ISAs for the economic modelling seem reasonable except with some of the more extreme ends of the sensitivity analyses. I have attached our recent Scottish Haematologist Guidelines for Follicular Lymphoma in which we have tried to address the approach to the unknown areas as outlined, in case the Review Group wish to compare our approach to the algorithms in the economic model

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