

**National Institute for Health and Clinical Excellence
Centre for Health Technology Evaluation**

Pro-forma Response

ERG report

**Bendamustine for the treatment of chronic lymphocytic
leukaemia**

Please find enclosed the ERG report prepared for this appraisal.

You are asked to check the ERG report from Peninsula Technology Assessment Group (PenTAG) to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 5pm, 22 October 2010 using the below proforma comments table. All factual errors will be highlighted in a report and presented to the Appraisal Committee and will subsequently be published on the NICE website with the Evaluation report.

The attached proforma document should act as a method of detailing any inaccuracies found and how and why they should be corrected.

29th October 2009

Issue 1 Confidential Information

Description of problem	Description of proposed amendment	Justification for amendment
<p>Napp Pharmaceuticals Ltd has removed the confidentiality status on the majority of the information in the submission document to increase the transparency of the decision process and therefore the identical information in the ERG report can be made publicly available.</p> <p>However please note that the overall survival curves will remain commercially in confidence at this stage due to this information not being released in the ASH abstract.</p>	<p>Remove confidentiality status from the ERG report according to the updated manufacturer's submission.</p> <p>Please ensure that within the ERG Report the following is kept confidential:</p> <ul style="list-style-type: none"> • Figure 6 page 43 • Figure 9 page 59 • Figure 10 page 80 • Tables on PFS and OS page 105 and page 106 	<p>Clarity and transparency in the decision making process.</p>

Issue 2 Cross referencing to submission document

Description of problem	Description of proposed amendment	Justification for amendment
<p>The cross references to the submission document in the ERG report refers to the original version of the document that Napp submitted to NICE on 12 August 2010. The original version of the submission was 239 pages.</p> <p>NICE requested that Napp produce a shorter version of the submission document as the original submission document was longer than normally permitted. Napp therefore produced a</p>	<p>We suggest that all references to the submission document in the ERG report are made to the shorter version of the submission document (sent 22nd October 2010). This means however, that the page numbers will need updating when cross referencing.</p>	<p>To save confusion, particularly when these documents are made publically available. Otherwise, it will be difficult following the ERG report when trying to match it to the submission document.</p>

<p>shorter version of the report (198 pages) which was sent to NICE on 26th August 2010.</p> <p>We understood that the shorter version of the submission document was going to be used for the remainder of the NICE appraisal process. An updated version of the shorter document was sent to NICE on 22nd October 2010 with most of the confidential information removed.</p>		
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Issue 3 Independent investigators were blinded

Description of problem	Description of proposed amendment	Justification for amendment
<p>On page 10 section 1.4.2, first bullet point, the description of independent investigators could be clarified</p>	<p>Add that the independent investigators were blinded</p>	<p>The point concerning bias is well made, however its impact is lessened by the fact that the independent investigators were blinded to treatment</p>

Issue 4 Assessment of progression by blinded investigators

Description of problem	Description of proposed amendment	Justification for amendment
<p>On page 32 section 4.1.7 there is some clarity required regarding the blinding of investigators when assessing progression</p>	<p>The ERG comments that it is likely that progression was assessed by non blinded investigators. The final study report states that 'Three independent experts were selected and reviewed blinded to treatment assignment all tumour evaluations per patient and agreed on the patients' best response and date of progression'</p>	<p>This correction gives the committee a more accurate picture in terms of likelihood of bias.</p>

Issue 5 NHL licence description

Description of problem	Description of proposed amendment	Justification for amendment
On page 18 of section 3.2 the description of the NHL indication within the licence is not complete	Please update the indication for indolent NHL by adding after the word treatment 'with rituximab or a rituximab containing regimen'	To quote the licensed indication exactly

Issue 6 Minor typo

Description of problem	Description of proposed amendment	Justification for amendment
In the last sentence of the last paragraph of page 52 of the ERG report there is a minor typo with the words 'face' and 'may' being in the incorrect order	We suggest that the sentence is rewritten to: 'Patients with PD <i>may face</i> second line treatment....'	Minor typo

Issue 7 Formatting error on page 65

Description of problem	Description of proposed amendment	Justification for amendment
There appeared to be a formatting error on page 63 of the report with a blank space and a caption Table 14 appearing before table 13.	Formatting to remove blank page and check table number etc.	Improves clarity

Issue 8 Study design filters

Description of problem	Description of proposed amendment	Justification for amendment
Medline in process study design filters pg. 21 were stated as being not included; this was not the case.	Please amend the sentence to say that the Medline in process searches did include a study design filter	To accurately reflect the search strategy