

CPAG Summary Report for Clinical Panel – Policy 1604
Bendamustine-based chemotherapy for treatment of relapsed or refractory Mantle Cell Lymphoma (MCL) in adults.

The Benefits of the Proposition			
<i>No</i>	<i>Outcome measures</i>	<i>Grade of evidence</i>	<i>Summary from evidence review</i>
1.	Survival	Not measured	<p>Overall Survival is a measure of how long following treatment patients are expected to live. It is not restricted to deaths that are disease-related; deaths of any cause are accounted for.</p> <p>In a study (Rummel et al 2016) with 219 patients with relapsed indolent (n=162) or mantle cell lymphoma (MCL), a type of cancer of the blood system, (n= 47), patients received rituximab and either bendamustine or fludarabine every 4 weeks for a maximum of 6 cycles.</p> <p>Median overall survival in the subgroup of patients with mantle cell lymphoma treated with bendamustine was 35.3 months vs. 20.9 months in the I group treated with fludarabine.</p> <p>The results suggest patients with mantle cell lymphoma treated with bendamustine can expect to live for about 14.4 months more compared to patients treat with fludarabine. The results are based on a study undertaken using a fairly robust methodology, however, it must be noted that the results described are based on a subgroup analysis i.e. evaluation of treatment effect in a patients with MCL. The study is also limited by the fact that the control regimen selected does not reflect current clinical practice. Also the results may not necessarily be generalisable to current practice in that</p>

			that when the study was started, rituximab was not routinely accepted as a standard treatment and so only 42% of patients recruited had been exposed to rituximab prior to recruitment to this study.
2.	Progression free survival	There is a survival benefit [B]	<p>Progression free survival is a measure of how long following treatment patients can expect to remain both alive and free of disease progression. Patients may not be disease or symptom free during this period</p> <p>In a study (Rummel et al 2016) with 219 patients with relapsed indolent (n=162) or MCL (n= 47), patients received rituximab and either bendamustine or fludarabine every 4 weeks for a maximum of 6 cycles.</p> <p>Median progression free survival in the subgroup of patients with MCL treated with bendamustine was reported to be 17.6 months (7.9 to 30.4) vs. 4.7 months (2.3 to 11.2) in the group treated with fludarabine.</p> <p>.</p> <p>The results suggest patients with MCL treated with bendamustine can expect to have a PFS of 12.9 months more compared to patients treat with fludarabine.</p> <p>Please see last paragraph in 'Summary from evidence review' for metric 1 – Survival for a commentary on uncertainties of evidence from Rummel et al (2016).</p>
3.	Mobility	Not measured	
4.	Self-care	Not measured	
5.	Usual activities	Not measured	
6.	Pain	Not measured	
7.	Anxiety / Depression	Not measured	

8.	Replacement of more toxic treatment	Not measured	
9.	Dependency on care giver / supporting independence	Not measured	
10.	Safety	Adverse events identified [B]	<p>In a study (Rummel et al 2016) with 219 patients with relapsed indolent (n=162) or MCL (n= 47) patients received rituximab and either bendamustine or fludarabine every 4 weeks for a maximum of 6 cycles.</p> <p>Grade 3/4 events reported as follows:</p> <ul style="list-style-type: none"> • Leucocytopenia, below normal levels of white blood cells (18% vs. 12% receiving fludarabine with rituximab) • Neutropenia, below normal levels of neutrophils, a type of white blood cells (9% vs. 9%) • Thrombocytopenia, below normal levels of platelets, cells that help with clotting of blood (3% vs. 2%) • Anaemia, d below normal levels of red blood cells (2% vs 2%) • Nausea/vomiting (4% vs 1%) • Fatigue (1% vs. 0) • Alopecia, hair loss (0 vs. 2%) <p>Please see last paragraph in 'Summary from evidence review' for metric 1 – Survival for a commentary on uncertainties of evidence from Rummel et al (2016).</p>
11.	Delivery of intervention	Not measured	

Other health outcome measures determined by the evidence review			
No	Outcome measure	Grade of evidence	Summary from evidence review
1	Overall response rate(OR) and Complete	Grade B	In a study (Rummel et al 2016) with 219 patients with relapsed indolent (n=162) or MCL (n= 47),patients

	response rates		<p>received rituximab and either bendamustine or fludarabine every 4 weeks for a maximum of 6 cycles.</p> <p>Overall response in the subgroup of patients with MCL was 70.8% in the group treated with bendamustine vs. 26.1% in the group treated with fludarabine. The corresponding CR rates were 37.5% and 13% respectively.</p> <p>The results suggest 44.7% more patients with MCL treated with bendamustine can expect to have an OR compared to patients treat with fludarabine.</p> <p>Please see last paragraph in 'Summary from evidence review' for metric 1 – Survival for a commentary on uncertainties of evidence from Rummel et al (2016).</p>
--	----------------	--	---