



COMPENDIA TRANSPARENCY TRACKING FORM

DATE: November 8, 2021

PACKET: 2141

DRUG: Bendamustine Hydrochloride

USE: Mantle cell lymphoma; Previously untreated, transplant ineligible, in combination with rituximab

COMPENDIA TRANSPARENCY REQUIREMENTS	
1	Provide criteria used to evaluate/prioritize the request (therapy)
2	Disclose evidentiary materials reviewed or considered
3	Provide names of individuals who have substantively participated in the review or disposition of the request and disclose their potential direct or indirect conflicts of interest
4	Provide meeting minutes and records of votes for disposition of the request (therapy)

EVALUATION/PRIORITIZATION CRITERIA: C, L, R, S \*to meet requirement 1

CODE	EVALUATION/PRIORITIZATION CRITERIA
A	Treatment represents an established standard of care or significant <b>advance</b> over current therapies
C	<b>Cancer</b> or cancer-related condition
E	Quantity and robustness of <b>evidence</b> for use support consideration
L	<b>Limited</b> alternative therapies exist for condition of interest
P	<b>Pediatric</b> condition
R	<b>Rare</b> disease
S	<b>Serious</b> , life-threatening condition

Note: a combination of codes may be applied to fully reflect points of consideration [eg, therapy may represent an advance in the treatment of a life-threatening condition with limited treatment alternatives (ASL)]



**EVIDENCE CONSIDERED:** \*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
<p>McKay, P, Leach, M, Jackson, B, et al: Guideline for the management of mantle cell lymphoma. Br J Haematol Jul 2018; Vol 182, Issue 1; pp. 46-62.</p>		S
<p>Dreyling M, Ghielmini M, Rule S, Salles G, Vitolo U, Ladetto M; ESMO Guidelines Committee. Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2016 Sep;27(suppl 5):v83-v90</p>		S
<p>Bhella, S, Varela, NP, Aw, A, et al: First-line therapy, autologous stem-cell transplantation, and post-transplantation maintenance in the management of newly diagnosed mantle cell lymphoma. Curr Oncol Dec 2020; Vol 27, Issue 6; pp. e632-e644.</p>		2
<p>Rummel,M.J., Niederle,N., Maschmeyer,G., et al: Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial.[Erratum appears in Lancet. Lancet Apr 06, 2013; Vol 381, Issue 9873; pp. 1203-1210.</p>	<p>This was an open-label, randomized phase 3 noninferiority trial that compared rituximab plus bendamustine versus R-CHOP in previously untreated patients with indolent and mantle-cell lymphomas. The risk of potential bias associated with randomization, allocation concealment, performance, attrition and reporting was deemed low. The risk of detection bias was deemed high risk due to the open-label nature of the study without the use of independent central review.</p>	S
<p>Flinn, IW, van der Jagt, R, Kahl, BS, et al: Randomized Trial of Bendamustine-Rituximab or R-CHOP/R-CVP in First-Line Treatment of Indolent NHL or MCL: The BRIGHT Study. Blood May 08, 2014; Vol 123, Issue 19; pp. 2944-2952.</p>	<p>This was an open-label, randomized phase 3 noninferiority trial that compared rituximab plus bendamustine versus R-CHOP or R-CVP in previously untreated patients with indolent and mantle-cell lymphomas. The primary outcome was response rate, assessed by a blinded review committee. The risk of potential bias associated with randomization, allocation concealment, performance, detection, attrition and reporting were deemed low.</p>	S



Flinn, IW, van der Jagt, R, Kahl, B, et al: First-Line Treatment of Patients With Indolent Non-Hodgkin Lymphoma or Mantle-Cell Lymphoma With Bendamustine Plus Rituximab Versus R-CHOP or R-CVP: Results of the BRIGHT 5-Year Follow-Up Study. J Clin Oncol Apr 20, 2019; Vol 37, Issue 12; pp. 984-991.		S
Chen, RW, Li, H, Bernstein, SH, et al: RB but not R-HCVAD is a feasible induction regimen prior to auto-HCT in frontline MCL: results of SWOG Study S1106. Br J Haematol Mar 2017; Vol 176, Issue 5; pp. 759-769.		3
Kamdar, M, Li, H, Chen, RW, et al: Five-year outcomes of the S1106 study of R-hyper-CVAD vs R-bendamustine in transplant-eligible patients with mantle cell lymphoma. Blood Adv Oct 22, 2019; Vol 3, Issue 20; pp. 3132-3135.		3
Merryman, RW, Edwin, N, Redd, R, et al: Rituximab/bendamustine and rituximab/cytarabine induction therapy for transplant-eligible mantle cell lymphoma. Blood Adv Mar 10, 2020; Vol 4, Issue 5; pp. 858-867.		2
Pezzullo, L, Giudice, V, Serio, B, et al: Real-world evidence of cytomegalovirus reactivation in non-Hodgkin lymphomas treated with bendamustine-containing regimens. Open Med (Wars) Apr 21, 2021; Vol 16, Issue 1; pp. 672-682.		1

Literature evaluation codes: S = Literature selected; 1 = Literature rejected = Topic not suitable for scope of content; 2 = Literature rejected = Does not add clinically significant new information; 3 = Literature rejected = Methodology flawed/Methodology limited and unacceptable; 4 = Other (review article, letter, commentary, or editorial)



**CONTRIBUTORS:**

\*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Megan Smith	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John Roberts	None
		Todd Gersten	None
		Richard LoCicero	Incyte Corporation:  Local PI for REVEAL. Study is a multicenter, non-interventional, non-randomized, prospective, observational study in an adult population for patients who have been diagnosed with clinically overt PV and are being followed in either community or academic medical centers in the US who will be enrolled over a 12-month period and observed for 36 months.

**ASSIGNMENT OF RATINGS:**

\*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
<b>IBM MICROMEDEX</b>	Effective	Class I: Recommended		B
Todd Gersten	Effective	Class I: Recommended	Phase III data reveal that Bendamustine (with Rituximab) has efficacy and tolerability that exceed that of other traditional chemotherapy combination regimens in this space.	
Richard LoCicero	Effective	Class I: Recommended	Phase III randomized trials and evidence-based consensus guidelines have established that bendamustine in combination with rituximab (in previously untreated, transplant ineligible patients) is effective and safe for the treatment of mantle cell lymphoma.	
John Roberts	Effective	Class I: Recommended	In a moderate-sized randomized trial of rituxamab plus bendamustine (BR) or either cyclophosphamide-doxorubicin-vincristine-prednisone (RCHOP) or cyclophosphamide-vincristine-prednisone (RCVP) depending upon the patient's clinical ability to tolerate RCHOP, BR was at least as effective and better tolerated than RCHOP/RCVP. BR was superior to RCHOP/RCVP in intermediate endpoints such as progression free survival.	