TRUVEN HEALTH ANALYTICS
an IBM Company

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 4/17/2018

PACKET: 1626

DRUG: Rituximab

USE: Mantle cell lymphoma untreated, maintenance therapy

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, S *to meet requirement 1

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

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Dreyling,M., et al: Newly diagnosed and relapsed mantle cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol Jul 01, 2017; Vol 28, Issue suppl 4; pp. iv62-iv71.		S
Nabhan,C., et al: A systematic review of comparative schedule-related toxicities with maintenance rituximab in follicular and mantle cell lymphomas. Leuk Lymphoma Jun 2014; Vol 55, Issue 6; pp. 1288-1294.	Comments: This was a systematic review that included five randomized trials assessing infectious complications in patients treated with rituximab maintenance therapy. This systematic review conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The appropriate statistical tests were used.	3
Aksoy,Sercan, et al: Infectious complications of rituximab in patients with lymphoma during maintenance therapy: a systematic review and meta-analysis. Leukemia & lymphoma Mar 2009; Vol 50, Issue 3; pp. 357-365	Comments: This was a systematic review that included five randomized trials assessing infectious complications in patients treated with rituximab maintenance therapy. This systematic review conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The appropriate statistical tests were used.	3
Kluin-Nelemans,H.C., et al: Treatment of older patients with mantle-cell lymphoma. New England journal of medicine 2012; Vol 367, Issue 6; pp. 520-531.	Comments: This was a multicenter, randomized phase 3 trial. Overall, the study was at low risk for selection bias, attrition bias, and reporting bias. For subjective outcomes, there was potentially high risk of bias for performance bias and detection bias due to the open-label design that did not use independent reviewers or assessors.	S

Le Gouill,S., et al: Rituximab after Autologous Stem-Cell Transplantation in Mantle-Cell Lymphoma. N.Engl.J Med Sep 28, 2017; Vol 377, Issue 13; pp. 1250-1260.	Comments: This was an open-label, randomized phase 3 trial. Overall, this study was at low risk of biases associated with lack of blinding (for objective outcomes only), incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with poor random sequence generation and allocation concealment was unclear and not discussed in the paper. For subjective outcomes, there was potentially high risk of bias for performance bias and detection bias due to the open-label design that did not use independent reviewers or assessors.	S
Rummel,M., et al: Bendamustine plus rituximab versus fludarabine plus rituximab for patients with relapsed indolent and mantle-cell lymphomas: a multicentre, randomised, open-label, non-inferiority phase 3 trial. Lancet Oncol Jan 2016; Vol 17, Issue 1; pp. 57-66.		1
Forstpointner,R., et al: Maintenance therapy with rituximab leads to a significant prolongation of response duration after salvage therapy with a combination of rituximab, fludarabine, cyclophosphamide, and mitoxantrone (R-FCM) in patients with recurring and refractory follicular and mantle cell lymphomas: Results of a prospective randomized study of the German Low Grade Lymphoma Study Group (GLSG). Blood Dec 15, 2006; Vol 108, Issue 13; pp. 4003-4008.	Comments: This was a multicenter, randomized phase 3 trial. Overall, the study was at low risk for selection bias, attrition bias, and reporting bias. For subjective outcomes, there was potentially high risk of bias for performance bias and detection bias due to the open-label design that did not use independent reviewers or assessors.	3

Ghielmini,Michele, et al: Effect of single-agent rituximab given at the standard schedule or as prolonged treatment in patients with mantle cell lymphoma: a study of the Swiss Group for Clinical Cancer Research (SAKK). <Py> Mar 1_2009 Feb 01, 2005; Vol 23, Issue 4; pp. 705-711.	Comments: This was a multicenter, randomized trial. Overall, the study was at low risk for selection bias, attrition bias, and reporting bias. For subjective outcomes, there was potentially high risk of bias for performance bias and detection bias due to the open-label design that did not use independent reviewers or assessors.	3
Dreyling,M., Geisler,C., Hermine,O., et al: Newly diagnosed and relapsed mantle cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol Sep 2014; Vol 25 Suppl 3, pp. iii83-iii92.		4
Caballero,D., et al: Clinical practice guidelines for diagnosis, treatment, and follow-up of patients with mantle cell lymphoma. Recommendations from the GEL/TAMO Spanish Cooperative Group. Annals of Hematology Sep 2013; Vol 92, Issue 9; pp. 1151-1179.		4
Vose,J.M.: Mantle cell lymphoma: 2017 update on diagnosis, risk-stratification, and clinical management. Am J Hematol Aug 2017; Vol 92, Issue 8; pp. 806-813.		4

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
Felicia Gelsey, MS	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John D Roberts	None
		Jeffrey Klein	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
MICROMEDEX	Effective	Class I: Recommended		B
John D Roberts	Effective	Class I: Recommended	Maintenance rituximab has been shown to improve outcomes including overall survival with acceptable toxicity when administered after remission induction with conventional or high dose therapy. Note: I have deleted the word "untreated" from the Submitted Use. None of the data addresses rituximab in untreated mantle cell lymphoma.	N/A
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of rituximab as a maintenance treatment for mantle cell lymphoma is effective with a true improvement with survival rates. Issues with infusion reactiona and adverse effects were downplayed by the authors of the studies it seems.	N/A

Richard LoCicero	Effective	Class I: Recommended	Prospective, randomized clinical trials have demonstrated that the Rituxan maintenance therapy after chemotherapy in elderly patients, and after autologous stem cell transplant in younger patients improves survival with acceptable toxicity.	N/A