TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: **June 2015**

PACKET: **1221**

DRUG: **Everolimus**

INDICATION: **Waldenstrom macroglobulinemia, relapsed or refractory**

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 *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
Ghobrial,I.M., Witzig,T.E., Gertz,M., et al: Long-term results of the phase II trial of the oral mTOR inhibitor everolimus (RAD001) in relapsed or refractory Waldenstrom Macroglobulinemia. American Journal of Hematology Mar 2014; Vol 89, Issue 3; pp. 237-242.	This was an open-label, single-arm, phase II trial. Overall, the quality of evidence was deemed low quality. Our confidence in the effect estimate is limited and the true effect may be substantially different from the estimate of the effect. The absence of a control group resulted in a high risk of bias. There was also high risk of bias associated with the open-label design for more subjective outcomes but not for overall survival. There was low risk of bias associated with selection of cohorts and attrition. Only one subject was lost to follow-up and not included in the analyses. Data was gathered prospectively for all outcomes.	S
Ghobrial,I.M., Gertz,M., Laplant,B., et al: Phase II trial of the oral mammalian target of rapamycin inhibitor everolimus in relapsed or refractory waldenstrom macroglobulinemia. Journal of Clinical Oncology Mar 10, 2010; Vol 28, Issue 8; pp. 1408-1414.		2
Dimopoulos,M.A., Kastritis,E., Owen,R.G., et al: Treatment recommendations for patients with Waldenstrom macroglobulinemia (WM) and related disorders: IWWM-7 consensus. Blood Aug 28, 2014; Vol 124, Issue 9; pp. 1404-1411.		S
Gertz,M.A.: Waldenstrom macroglobulinemia: 2015 update on diagnosis, risk stratification, and management. American Journal of Hematology Apr 01, 2015; Vol 90, Issue 4; pp. 346-354.		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
Margi Schiefelbein, PA	None	Edward Balaban, DO	None
Stacy LaClaire, PharmD	None	James E. Liebmann, MD	None
Felicia Gelsey, MS	None	Jeffrey A. Bubis, DO	None
		Keith Thompson, MD	None
		Jeffrey Patton, MD	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---			B
Edward Balaban, DO	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	Although there is not much clinical experience to reflect on – what is available looks promising, but with substantial toxicity.	N/A
James E. Liebmann, MD	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	The Ghobrial study is small, but does show an impressive response rate in a group of heavily pretreated patients. However, side effects of everolimus can be formidable (2/3 of patients had ≥ grade 3 toxicity and required dose reductions or delays) and there are no data comparing everolimus with other treatments. I believe the use of everolimus in this setting is best summarized by the Dimopoulos report, “everolimus may…be considered for selected patients with relapsed or refractory disease and limited options.”	N/A

Jeffrey A. Bubis, DO	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	The agent was active in a single agent trial of patients with refractory disease. Use in patients with relapsed/refractory disease is reasonable.	N/A
Keith Thompson, MD	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	None	N/A
Jeffrey Patton, MD	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	None	N/A