IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: October 25, 2021

PACKET: 2130

DRUG: Ixazomib

USE: Waldenström macroglobulinemia; In combination with rituximab and dexamethasone

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, E, R, 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)]

EVIDENCE CONSIDERED: *to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Castillo, JJ, Advani, RH, Branagan, AR, et al: Consensus treatment recommendations from the tenth International Workshop for Waldenstrom Macroglobulinaemia. Lancet Haematol Nov 2020; Vol 7, Issue 11; pp. e827-e837.		S
Kersten MJ, Amaador K, Minnema MC, et al. Combining Ixazomib With Subcutaneous Rituximab and Dexamethasone in Relapsed or Refractory Waldenström's Macroglobulinemia: Final Analysis of the Phase I/II HOVON124/ECWM-R2 Study. J Clin Oncol. 2021 Aug 13:JCO2100105. Epub ahead of print.	This was a prospective single-arm phase 2 clinical trial that investigated ixazomib in patients with relapsed or refractory Waldenström's macroglobulinemia. The risk of bias due to confounding, selection, classification of and deviation from intervention, missing data, measurement of outcome, and selective reporting were deemed low risk. A major caveat of the study is the lack of a control group.	S
Castillo, JJ, Meid, K, Gustine, JN, et al: Prospective clinical trial of ixazomib, dexamethasone, and rituximab as primary therapy in Waldenstrom macroglobulinaemia. Clin Cancer Res Jul 15, 2018; Vol 24, Issue 14; pp. 3247-3252.	This was a prospective single-arm phase 2 clinical trial that investigated ixazomib and dexamaethasone in patients with previously untreated Waldenström's macroglobulinemia. The risk of bias due to confounding, selection, classification of and deviation from intervention, and missing data were deemed low risk. The risk of bias associated with measurement and selection of outcome were deemed high risk due to the primary outcome being investigator-assessed and overall response. A major caveat of the study is the lack of a control group.	S
Castillo, JJ, Meid, K, Flynn, CA, et al: Ixazomib, dexamethasone, and rituximab in treatment-naive patients with Waldenström macroglobulinemia: long-term follow-up. Blood Adv Aug 25, 2020; Vol 4, Issue 16; pp. 3952-3959.		S

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
IBM MICROMEDEX	Effective	Class IIa: Recommended, in Most Cases		B
Todd Gersten	Effective	Class IIb: Recommended, in Some Cases	This three drug combination has demonstrated efficacy, per Phase II studies in both front line and relapsed settings, on par with a long list of other treatment options for WM.	
Richard LoCicero	Effective	Class IIa: Recommended, in Most Cases	The combination of ixazomib, rituximab and dexamethasone has been shown to effective and safe in the treatment of Waldenstrom macroglobulinemia in phase II trials.	
John Roberts	Effective	Class I: Recommended	In single arm studies in both previously untreated and previously treated patients living with Waldenstrom macroglobulinemia the combination of ixazomib + rituximab + dexamethasone was active and well-tolerated. Of note, neuropathy was not a significant toxicity. The combination is one of many treatment options, among which there is little evidence base upon which to make comparisons.	