IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 10/3/2019

PACKET: 1617

DRUG: Vemurafenib

USE: Malignant melanoma; Adjuvant therapy, cutaneous, with BRAF-V600 mutation

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 **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
Maio, M, Lewis, K, Demidov, L, et al: Adjuvant vemurafenib in resected, BRAFV600 mutation-positive melanoma (BRIM8): a randomised, double-blind, placebo-controlled, multicentre, phase 3 trial. Lancet Oncol Apr 2018; Vol 19, Issue 4; pp. 510-520.	This was a double-blind, placebo-controlled, randomized Phase 3 trial that assessed vemurafenib versus placebo in patients with resected BRAF-V600 mutation-positive melanoma. The risk of potential bias associated with randomization, allocation concealment, performance, detection, attrition, and reporting were deemed low. No other sources of bias were found.	S
van Zeijl,M.C.T., van den Eertwegh,A.J., Haanen,J.B., et al: (Neo)adjuvant systemic therapy for melanoma. European Journal of Surgical Oncology 2017; Vol 43, Issue 3; pp. 534-543.		4
Romero, D: Melanoma: time for adjuvant vemurafenib?. Nat Rev Clin Oncol May 2018; Vol 15, Issue 5; p. 265.		4
Warner, AB and Postow, MA: The brim of uncertainty in adjuvant treatment of melanoma. Lancet Oncol Apr 2018; Vol 19, Issue 4; pp. 436-437.		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
Megan Smith	None		
Stacy LaClaire, PharmD	None		
Margi Schiefelbein, PA	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
IBM MICROMEDEX	Evidence is Inconclusive	Class III: Not Recommended		B
Richard LoCicero	Evidence is Inconclusive	Class III: Not Recommended	The predefined trial design of the phase III trial evaluating the use of vemurabenib as adjuvant treatment for stage IIC and stage III melanoma resulted in statistically inconclusive evidence of efficacy.	

John Roberts	Evidence is Inconclusive	Class III: Not Recommended	On the basis of a single large randomized placebo controlled trial with prospective stratification by clinical stage, it seems likely that vemurafanib as an adjuvant therapy in BRAF-V600 mutated cutaneous melanoma may modestly prolong disease free survival some stages. Whether due to the study design, bad luck, or underlying biology, the data do not allow one to target the treatment for this indication with confidence. No survival benefit has been seen to date in relatively immature data. The treatment is moderately toxic. Available data do not support its use for this indication.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The use of vemurafenib as adjuvant therapy for malignant melanoma shows a good degree of effectiveness depending on the patient type. The adverse effect profile is not very favorable when compared to placebo.	