TRUVEN HEALTH ANALYTICS
an IBM Company

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 12/20/2017

PACKET: 1610

DRUG: Dabrafenib

USE: Malignant melanoma, Adjuvant, following complete resection of Stage III (with lymph node involvement greater than 1 mm) disease with BRAF V600E or V600K mutation, in combination with trametinib

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
Long,G.V., Hauschild,A., Santinami,M., et al: Adjuvant dabrafenib plus trametinib in stage III BRAF-mutated melanoma. N Engl J Med Sep 10, 2017; Vol Epub, p. Epub.	Comments: This was a randomized, double-blind, phase 3 trial with 169 sites in 26 countries. Key bias criteria evaluated were (1) random sequence generation of randomization; (2) lack of allocation concealment, (3) lack of blinding, (4) incomplete accounting of patients and outcome events, and (5) selective outcome reporting bias. The study was at low risk of bias for these key criteria, and no additional biases were identified.	S
Ben-Ami,E. and Schachter,J.: Adjuvant treatment for stage III melanoma in the era of targeted medicine and immunotherapy. Melanoma Management Jun 01, 2016; Vol 3, Issue 2; pp. 137-147.		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	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases		B
John D Roberts	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	Dabrafenib in combination with tremetinib as adjuvant therapy for resected Stage III (lymph node involvement > 1 mm) significantly prolonged progression free survival. Results to date show a trend toward prolongation of overall survival. Treatment was moderately toxic with 1/4 of patients discontinuing treatment earlier than planned.	N/A
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	The use of Dabrafenib with trametinib showed some effectiveness to decrease recurrence of metastatic melanoma following resection. Those patients tested were stage III and exhibited specific gene mutations. The study was somewhat small and grade 3,4 adverse effects were significant in prevalence (though the study authors downplay the incidence). One has to wonder if testing for these exact mutations would be available to all patients as well be covered under insurance or reasonably priced.	N/A
Richard LoCicero	Effective	Class I: Recommended	The combination of dabrafenib and trametinib was evaluated in a double-blind, placebo-controlled, phase 3 trial in patient with Stage III melanoma (with BRAF V600E or V600K mutations). The treatment arm was associated with improved 3-year relapse free survival compared with the placebo group (58% vs. 39%). No new toxicities were identified.	N/A