IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 11/16/2020

PACKET: 2046

DRUG: Regorafenib

USE: Osteosarcoma of bone; Metastatic or advanced, progressive, previously treated

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: A, 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
Casali, PG, Bielack, S, Abecassis, N, et al: Bone sarcomas: ESMO-PaedCan-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol Oct 01, 2018; Vol 29, Issue Suppl 4; pp. iv79-iv95.		S
Duffaud, F, Mir, O, Boudou-Rouquette, P, et al: Efficacy and safety of regorafenib in adult patients with metastatic osteosarcoma: a non-comparative, randomised, double-blind, placebo-controlled, phase 2 study. Lancet Oncol Jan 2019; Vol 20, Issue 1; pp. 120-133.	This was part of a double-blind, placebo-controlled, randomized phase II basket trial that assessed regorafenib in patients with different types of sarcoma. This report pertains to the results for the osteosarcoma cohort. The risk of potential bias associated with randomization, allocation concealment, performance, detection, attrition, and reporting were deemed low. An additional potential source of bias - funding bias - was deemed low risk as well.	S
Davis, LE, Bolejack, V, Ryan, CW, et al: Randomized Double-Blind Phase II Study of Regorafenib in Patients With Metastatic Osteosarcoma. J Clin Oncol Jun 01, 2019; Vol 37, Issue 16; pp. 1424-1431.	This was part of a double-blind, placebo-controlled, randomized phase II basket trial that assessed regorafenib in patients with different types of sarcoma. Davis et al report the results for the osteosarcoma cohort. The risk of potential bias associated with performance, detection, attrition, and reporting were deemed low. The risk of potential bias associated with randomization and allocation concealment was deemed unclear due to the lack of information on these methods. An additional potential source of bias - funding bias - was deemed unclear risk due to lack of specific details.	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 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 Favors Efficacy	Class IIb: Recommended, in Some Cases		B
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The use of Regorafenib for previously treated metastatic osteosarcoma patients shows a good degree of progression free survival. The studies were small and were conducted over a few years. The high rate of serious adverse effects is somthing that needs to be considered.	

John Roberts	Evidence is Inconclusive	Class III: Not Recommended	Results from 2 small randomized phase II trials show occasional responses and modest increases in disease free survival, with moderate toxicity, with regorafinib in advanced, previously treated osteosarcoma. Neither study shows a survival benefit; the point estimate for median survival was greater for placebo in 1 trial; assessment of survival was confounded in both trials by a significant number of cross-overs among patients originally treated with placebo. These data do not justify treating patients with regorafinib outside of a study setting.	
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	At least two phase II trials have demonstrated the activity of regorafenib in the treatment of advanced, progressive, previously treated osteosarcoma, without unexpected toxicity. Current ESMO-PaedCan-EURACAN evidence-based clinical practice guidelines support the use of regorafenib in this setting as well.	