TRUVEN HEALTH ANALYTICS
an IBM Company

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 10/16/2018

PACKET: 1771

DRUG: Nintedanib

USE: Non-small cell lung cancer, Stage IIIB or IV disease, as second-line therapy in combination

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 *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
Reck,M., Kaiser,R., Mellemgaard,A., et al: Docetaxel plus nintedanib versus docetaxel plus placebo in patients with previously treated non-small-cell lung cancer (LUME-Lung 1): a phase 3, double-blind, randomised controlled trial. Lancet Oncol Feb 2014; Vol 15, Issue 2; pp. 143-155.	Comments: The LUME-Lung 1 trial was an international, double-blind, randomized, placebo-controlled, phase III trial that was conducted in 211 sites in 27 countries (23 European countries, China, South Korea, India, and South Africa). 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
Hanna,N.H., Kaiser,R., Sullivan,R.N., et al: Nintedanib plus pemetrexed versus placebo plus pemetrexed in patients with relapsed or refractory, advanced non-small cell lung cancer (LUME-Lung 2): a randomized, double-blind, phase III trial. Lung Cancer Dec 2016; Vol 102, pp. 65-73.	Comments: The LUME-Lung 2 trial was an international, randomized, placebo-controlled, phase III trial that was conducted in parallel to LUME-Lung 1 to assess whether using nintedanib plus pemetrexed (nintedanib–pemetrexed) for previously treated patients with advanced or recurrent, non-squamousNSCLC led to greater efficacy than using pemetrexed alone. The study included 202 sites in 32 countries (North and South America, Europe, Asia and Australia/Oceania). The results of a pre-planned futility analysis conducted by the independent DMC using the investigator-assessed PFS, suggested that the study was unlikely to reach the predefined efficacy criteria for the primary endpoint according to the protocol, and led to their recommendation that study enrollment be stopped. Overall, this study was at low risk of biases associated with lack of blinding for objective outcomes, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with poor random sequence generation and allocation concealment was unclear and not discussed in the paper.	S
Espinosa,Bosch M., Asensi,Diez R., Garcia,Agudo S., et al: Nintedanib in combination with docetaxel for second-line treatment of advanced non-small-cell lung cancer; GENESIS-SEFH drug evaluation report. Farm Hosp Jun 01, 2016; Vol 40, Issue 4; pp. 316-327.		4

Novello,S., Kaiser,R., Mellemgaard,A., et al: Analysis of patient-reported outcomes from the LUME-Lung 1 trial: a randomised, double-blind, placebo-controlled, phase III study of second-line nintedanib in patients with advanced non-small cell lung cancer. Eur J Cancer Feb 2015; Vol 51, Issue 3; pp. 317-326.	Comments: The LUME-Lung 1 trial was an international, double-blind, randomized, placebo-controlled, phase III trial that was conducted in 211 sites in 27 countries (23 European countries, China, South Korea, India, and South Africa). 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
Novello,S., Barlesi,F., Califano,R., et al: Metastatic non-small-cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol Sep 2016; Vol 27, Issue suppl 5; pp. v1-v27.		S
Hall,C.J., Hay,N., George,E., et al: NICE guidance on nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer. Lancet Oncol Sep 2015; Vol 16, Issue 9; pp. 1019-1020.		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	Ineffective	Class III: Not Recommended		B
John D Roberts	Ineffective	Class III: Not Recommended	A neglible survival benefit with modest increased toxicity has been shown with the addition of nintedanib to docetaxel as second line treatment for adenomatous non-small lung cancer. No benefit is apparent in squamous non-small cell lung cancer.	N/A

Jeffrey Klein	Ineffective	Class lll: Not Recommended	Adding Ninetedanib to other chemotherapeutic agents to manage NSCLC showed no significant benefit to warrant its use in the survival category or progreesion free area. The additional adverse effects with this therapy warrants a strong look when considering this therapy.	N/A
Richard LoCicero	Evidence is Inconclusive	Class lll: Not Recommended	No significant clinical benefit was observed in clinical trials evaluating nintedanib in combination with docetaxel in second line treatment of NSCLC. Toxicity was increased.	N/A