COMPENDIA TRANSPARENCY TRACKING FORM

DATE: **January 2016**

PACKET: **1231**

DRUG: **Afatinib Dimaleate**

USE: **Squamous cell carcinoma of the head and neck, Recurrent and/or metastatic disease, second-line as monotherapy after failure of platinum-based therapy**

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
Machiels,J.P., et al: Afatinib versus methotrexate as second-line treatment in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck progressing on or after platinum-based therapy (LUX-Head & Neck 1): an open-label, randomised phase 3 trial. Lancet Oncol May 2015; Vol 16, Issue 5; pp. 583-594	Comments: This was a randomized controlled trial. 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
Seiwert,T.Y., et al: A randomized, phase II study of afatinib versus cetuximab in metastatic or recurrent squamous cell carcinoma of the head and neck. Ann Oncol Sep 2014; Vol 25, Issue 9; pp. 1813-1820.	Comments: This was an international, open-label, randomized-controlled trial. Overall, this study was at low risk for most of the key risk of bias criteria which included lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with random sequence generation and allocation concealment was unclear and not discussed in the paper; however, this was an international trial conducted in 43 centers in Belgium, France, Spain, and US so the risk of bias was probably low.	3
Killock,D.: Head and neck cancer: Second-line afatinib shows promise. Nat Rev Clin Oncol Jul 2015; Vol 12, Issue 7; p. 373.		4
Ferrarotto,R. and Gold,K.A.: Afatinib in the treatment of head and neck squamous cell carcinoma. Expert Opin Investig Drugs Jan 2014; Vol 23, Issue 1; pp. 135-143.		4

Burtness,B., et al: LUX head and neck 2: A randomized, double-blind, placebo-controlled, phase III study of afatinib as adjuvant therapy after chemoradiation in primarily unresected, clinically high-risk, head and neck cancer patients. Journal of Clinical Oncology 2012; Vol 30, Issue 15 SUPPL. 1.	This is an abstract.	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	John D Roberts	None
Stacy LaClaire, PharmD	None	Richard LoCicero	None
Catherine Sabatos, PharmD	None	Mark Levin	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases		B
John D Roberts	Ineffective	Class III: Not Recommended	Although methotrexate often is used as a second line therapy, there is no evidence that it is superior to best supportive care; and, given low response rates and a significant mucositis burden, it is quite possible that it is inferior to best supportive care. Consistent with this position, NCCN guidelines recommend best supportive care, not second line chemotherapy, for PS 2-3 patients, and systemic therapy, clinical trial preferred, or best supportive care for PS 0-1 patients. Thus, although a recent report demonstrates that afatinib is marginally superior than methotrexate, it does not necessarily follow that afatinib is effective, that is, superior to best supportive care. Indeed, given a ~30% frequency of grade 3 toxicity, it is quite possible that afatinib is inferior to best supportive care.	N/A

Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	Afatinib therapy prolonged progression-free survival (primary endnpoint), but overall survival (secondary endpoint) was not improved. Afatanib was well tolerated, with similar efficacy to an existing standard of care (methotrexate).	N/A
Mark Levin	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	This drug has efficacy as single agent. It will probably find its place in relapsed and refractory patients. There remains some lack of clarity how to use it in combinations, which is where all leukemia treatments must find a place in order to be accepted. In combination with retinoic acid Even now, it is most useful in relapsed and refractory cases, which is why I selected Class IIa. Recent studies show that Afatinib prolongs Progression Free survival with lesser toxicity that is common with the second line chemotherapy methotrexate. However, the real question is how it works int his setting with more recent and more effective drugs than methotrexate. It is clearly appropriate in some cases of relapsed and refractory disease because it is an effective drug.	N/A