

Submitted by:

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NCCN Guidelines Panel: Head & Neck Cancer

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On behalf of Boehringer-Ingelheim Pharmaceuticals, Inc., I respectfully request the NCCN Head & Neck Cancer Guidelines Panel to review the enclosed data for inclusion of Afatinib (Gilotrif™) for second line treatment of recurrent or metastatic (R/M) squamous-cell carcinoma of the head and neck (HNSCC).

Specific Changes: Add Afatinib (Gilotrif™) for:

- Second line treatment of R/M HNSCC after failure of platinum based therapy.

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Rationale: In the randomized controlled phase III LUX-Head and Neck 1 trial, oral afatinib significantly improved progression free survival (PFS) versus intravenous methotrexate in patients with squamous cell carcinoma of the head and neck (HNSCC) who had progressed on or after single previous platinum based chemotherapy in the recurrent or metastatic (RM) setting, reducing the risk for disease progression by 20%. In addition, the PFS improvement was associated with patient reported outcomes (PRO) benefit. The adverse event profile was as expected with both treatment arms, but favored afatinib in terms of fewer treatment-related dose reductions, discontinuations and fatal events. In a subgroup, pronounced PFS benefit was noted in patients who had not previously been treated with an EGFR inhibitor and in those with human papillomavirus (HPV) negative tumors.

In a randomized phase II trial of afatinib versus cetuximab in metastatic or recurrent squamous cell carcinoma of the head and neck after failure of platinum based therapy, afatinib demonstrated comparable activity to cetuximab in terms of tumor shrinkage, progression free survival (PFS), disease control rate (DCR) and overall response rate (ORR) in patients with recurrent or metastatic (RM) squamous cell carcinoma of the head and neck (HNSCC). Sequential EGFR/ErbB treatment with afatinib and cetuximab provided sustained clinical benefit in patients after crossover, suggesting a lack of cross-resistance.

The following articles are submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of this publication.

1. Machiels J-PH, Haddad RI, Fayette J, et al, for the LUX-H&N 1 investigators. 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* 2015; 16, 5:583-594
2. Seiwert TY, Fayette J, Cupissol D, 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* 2014; 25: 1813–20.

FDA clearance: On July 12, 2014 the FDA cleared the use of Afatinib for the first line treatment of patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA – approved test. This approval includes the following limitation of use: Safety and efficacy of Gilotrif have not been established in patients whose tumors have other EGFR mutations.

Sincerely,



Elizabeth Terlizzi