Name: Dr. Thomas Lechner, MS, PhD

Therapeutic Area Head Oncology

Interim Head, Clinical Development and Medical Affairs, Specialty Care

Company/Organization: Boehringer-Ingelheim Pharmaceuticals, Inc.

Address: 900 Ridgebury Road

Ridgefield, CT. 06877-0368

Phone: 203 219 6158

Email: thomas.lechner@boehringer-ingelheim.comRe: :

Re: NCCN Guidelines Panel: Non-Small Cell Lung Cancer

Dear Dr. Ettinger,

On behalf of Boehringer-Ingelheim Pharmaceuticals, Inc., I respectfully request the NCCN Non-Small Cell Lung Cancer Guidelines Panel to review and consider the enclosed data for inclusion of afatinib (Gilotrif™) for treatment of advanced squamous cell carcinoma of the lung following progression on or after platinum based chemotherapy.

Specific Changes: Add afatinib (Gilotrif™) for subsequent therapy for the treatment of patients with advanced squamous cell carcinoma of the lung (SCC) following progression on or after platinum based chemotherapy.

Rationale:

Despite the FDA approval of afatinib for patients with SCC, many payers still deny access to afatinib by not including this indication in their guidelines. This lead to instances where appropriate patients, despite therapy decisions taken by their physicians had access to afatinib denied due to the payers' decision to only include therapies on formulary noted in the NCCN guidelines.

Afatinib was approved based on results from the phase III LUX-Lung 8 trial which randomized erlotinib and afatinib in patients with advanced squamous cell carcinoma of the lung following platinum based chemotherapy. The results of this study showed that treatment with afatinib improved both progression free survival and overall survival as compared to treatment with erlotinib. Afatinib was also associated with improvements in disease control rate, patient related outcomes, and disease-related symptoms versus erlotinib. The pattern of adverse events was similar between treatments and consistent with their already established safety profile.

In addition, in a retrospective analysis of the phase III LUX-Lung 8 trial the ability of the VeriStrat serum protein test to predict differential clinical benefit with afatinib versus erlotinib, and the association of VeriStrat status with clinical outcomes irrespective of EGFR-TKI used, was assessed. Pretreatment plasma samples were analyzed using matrix-assisted laser desorption ionization time-of-flight mass spectrometry. Spectra were evaluated to assign a VeriStrat 'Good' (VS-G) or VeriStrat 'Poor' (VS-P) classification. Overall survival (OS), progression-free survival, and other endpoints were assessed with respect to pretreatment VeriStrat status. OS was the primary efficacy variable. VS-G classification is strongly associated with favorable survival outcomes with either afatinib or erlotinib compared with VS-P classification. In VS-G patients, survival outcomes with afatinib were superior to those with erlotinib.

FDA initially approved afatinib in 2013 for the 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 and in 2016 for metastatic, squamous NSCLC progressing after platinum-based chemotherapy.

The most recent Supplemental NDA approval (January 12, 2018) from the FDA for GILOTRIF (afatinib) tablets broadens GILOTRIF's (afatinib) indication as a first-line treatment for patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test.

The following publications are submitted in support of this proposed change.

Afatinib (A) vs erlotinib (E) as second-line therapy of patients (pts) with advanced squamous cell carcinoma (SCC) of the lung following platinum-based chemotherapy: overall survival (OS) analysis from the global phase III trial LUX-Lung 8 (LL8), J.C. Soria et al

Gadgeel S, Goss G, Soria JC, et al. Evaluation of the VeriStrat® serum protein test in patients with advanced squamous cell carcinoma of the lung treated with second-line afatinib or erlotinib in the phase III LUX-Lung 8 study. Lung Cancer. 2017;109:101-108. Free full text available at: https://www.ncbi.nlm.nih.gov/pubmed/28577938.

Sincerely,

Thomas Lechner MS, PhD

Therapeutic Area Head Oncology

Interim Head, Clinical Development and Medical Affairs, Specialty Care

Boehringer-Ingelheim Pharmaceuticals, Inc