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NCCN Guidelines Panel: Non-Small Cell Lung Cancer (NSCLC)

Dear NCCN NSCLC Panel Members,

On behalf of Pfizer Oncology, I respectfully request the NCCN Guideline Panel for Non-Small Cell Lung Cancer (NSCLC) to review the enclosed information for inclusion of VIZIMPRO (dacomitinib) for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations.

**Specific Changes Requested: Recommend the addition of VIZIMPRO (dacomitinib) as a first-line therapy for patients with sensitizing *EGFR* mutation positive metastatic NSCLC.**

FDA Approval: On September 27, 2018, the FDA approved VIZIMPRO (dacomitinib), a kinase inhibitor, for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

Rationale: Based on the FDA-approved indication and data from the ARCHER 1050 trial (NCT01774721), VIZIMPRO (dacomitinib) demonstrated statistically significant improvement in progression-free survival (PFS) as determined by blinded independent radiologic committee (IRC) review compared with gefitinib in patients with advanced EGFR mutation-positive NSCLC.

**The following resources are submitted in support of this requested change:**

1. VIZIMPRO (dacomitinib) prescribing information. Pfizer Inc.
2. Wu YL, Cheng Y, Zhou X, et al. Dacomitinib versus gefitinib as first-line treatment for patients with EGFR-mutation-positive non-small-cell lung cancer (ARCHER 1050): a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2017;18:1454-1466.

The basis for the approval was an international, multicenter, randomized, open-label, phase 3 trial (ARCHER 1050), which evaluated the efficacy and safety of dacomitinib versus gefitinib as first-line therapy in patients with advanced EGFR-mutation-positive NSCLC.

Patients were required to have unresectable, metastatic NSCLC with no prior therapy for metastatic disease or recurrent disease with a minimum of 12 months disease-free after completion of systemic therapy; an Eastern



Cooperative Oncology Group (ECOG) performance status of 0 or 1; EGFR exon 19 deletion or exon 21 L858R substitution mutations. A total of 452 patients were randomized (1:1) to receive VIZIMPRO 45 mg orally once daily (N=227) or gefitinib 250 mg orally once daily (N=225) until disease progression or unacceptable toxicity. The primary endpoint was PFS as determined by blinded IRC review per RECIST v1.1. Additional efficacy outcome measures were overall response rate (ORR), duration of response (DoR), and overall survival (OS). The hierarchical statistical testing order was PFS followed by ORR and then OS. No formal testing of OS was conducted since the formal comparison of ORR was not statistically significant. A statistically significant improvement in PFS as determined by the IRC was demonstrated for patients randomized to VIZIMPRO compared with gefitinib (HR = 0.59 [95% CI: 0.47, 0.74],  $p < 0.0001$ ). Median PFS in the VIZIMPRO group was 14.7 months (95% CI: 11.1, 16.6) compared with 9.2 months (95% CI: 9.1, 11.0) in the gefitinib arm.

The most common (>20%) adverse reactions were diarrhea (87%), rash (69%), paronychia (64%), stomatitis (45%), decreased appetite (31%), dry skin (30%), decreased weight (26%), alopecia (23%), cough (21%), and pruritus (21%). The most common ( $\geq 1\%$ ) serious adverse reactions were diarrhea (2.2%) and interstitial lung disease (1.3%).

We greatly appreciate the Panel's thorough consideration of the data for VIZIMPRO (dacomitinib) as a first-line therapy for patients with sensitizing *EGFR* mutation positive metastatic NSCLC.

Best regards,

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