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Date of request: January 31, 2012
NCCN Guidelines Panel: Kidney / Testicular Cancer

Dear Ms. McClure,

On behalf of the Oncology Business Unit at Pfizer Inc, I am submitting the following to the NCCN Guidelines Panel requesting the Panel's consideration for inclusion in the NCCN Compendia listings.

- **Request for NCCN Guidelines Panel to consider review of data for a specific indication**
  - INLYTA (axitinib) is indicated for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.
- **Specific changes recommended within the NCCN Guidelines (one sentence)**
  - For patients with advanced renal cell carcinoma who have failed at least one prior systemic therapy that treatment with INLYTA (axitinib) gets listed as a treatment option (category 1).
- **Statement of whether the submitted use is or is not FDA approved for that indication**
  - The submitted use was approved by the FDA for this indication on January 27, 2012.
- **Rationale for recommended change (one sentence)**
  - Patients with advanced renal cell carcinoma who have failed at least one prior systemic therapy have few approved treatment options.
- **Citation of literature support and complete articles supporting recommended change:**

  - Rini BI, Escudier B, Tomczak P, et al. Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial. The Lancet 2011;378:1931-9.
  - Rini BI, Wilding G, Hudes G, et al. Phase II study of axitinib in sorafenib-refractory metastatic renal cell carcinoma. J Clin Oncol 2009; 27: 4462–68.
  - Rixe O, Bukowski RM, Michaelson MD, et al. Axitinib treatment in patients with cytokine-refractory metastatic renal-cell cancer: a phase II study. Lancet Oncol 2007; 8: 975–84.
  - Tomita Y, Uemura H, Fujimoto H, et al. Key predictive factors of axitinib (AG-013736)-induced proteinuria and efficacy: a phase II study in Japanese patients with cytokine-refractory metastatic renal cell Carcinoma. Eur J Cancer. 2011;47:2592-602.

On January 27, 2012, the FDA approved INLYTA (axitinib) for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy. The basis for the approval was the randomized phase 3 study comparing axitinib with sorafenib in patients with renal cell carcinoma who progressed following first-line therapy containing sunitinib, bevacizumab plus interferon-alfa, temsirolimus, or cytokines.

A total of 723 patients were enrolled and randomly assigned to receive axitinib (n=361) or sorafenib (n=362). The study met the primary endpoint, progression-free survival (PFS) as assessed by independent review: median PFS was 6·7 months with axitinib compared to 4·7 months with sorafenib (hazard ratio

0·665; 95% CI 0·544–0·812; one-sided p<0·0001). For the patients who received sunitinib as prior therapy, there was a 25.9% reduction in the hazard of disease progression or death (HR = 0.741; p-value <0.0107) for the axitinib arm vs the active comparator, sorafenib. For the patients who received prior-cytokine therapy, there was a 53.6% reduction in the hazard of disease progression or death (HR = 0.464; p-value <0.0001) for the axitinib versus sorafenib.

AEs were generally tolerable and clinically manageable. There was an increased incidence of hypertension, nausea, dysphonia, and hypothyroidism for patients in the axitinib arm compared with the sorafenib arm, and an increased incidence of palmar-plantar erythrodysesthesia syndrome, rash, and alopecia for patients in the sorafenib arm compared with the axitinib arm.

In addition to the Phase III data, the nonclinical data, and data from Phase I and Phase II trials (articles attached) support the mechanism of action, clinical safety, and clinical efficacy of axitinib in patients with advanced renal cell carcinoma.

We appreciate the Panel's thorough consideration of Pfizer's submission for INLYTA (axitinib) for the treatment of patients advanced RCC after failure of one prior systemic therapy.

Sincere regards,

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