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Date of request: June 30, 2020

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NCCN Guidelines Panel: Bladder Cancer

Dear NCCN Bladder Cancer Panel Members,

On behalf of the Pfizer and EMD Serono Alliance, we respectfully request the NCCN Guideline Panel for Bladder Cancer to review the enclosed information for inclusion of avelumab as first-line maintenance therapy in patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with platinum-containing chemotherapy.

Specific Changes Requested: Recommend the addition of avelumab as a first-line maintenance therapy for patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with platinum-containing chemotherapy.

FDA Clearance (Urothelial Carcinoma):

First-Line Maintenance Treatment of Urothelial Carcinoma
Avelumab (BAVENCIO®) is indicated for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy

Rationale: Based on the data from the JAVELIN Bladder 100 trial (NCT02603432), avelumab plus best supportive care (BSC) demonstrated statistically significant improvement in overall survival (OS) compared with BSC alone in patients with urothelial carcinoma whose disease had not progressed with first-line platinum-based chemotherapy in both the overall population and in patients with PD-L1+ tumors.

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

1. BAVENCIO® (avelumab) prescribing information, EMD Serono, Inc. and Pfizer, Inc., June 2020

The basis for this request are the results from an international, multicenter, randomized, open-label, phase 3 trial (JAVELIN Bladder 100), which evaluated the efficacy and safety of avelumab plus BSC versus BSC alone as first-line maintenance therapy in patients with unresectable locally advanced or metastatic urothelial cancer whose disease has not progressed with platinum-based induction chemotherapy.

Patients were required to have measurable, unresectable, locally advanced or metastatic urothelial carcinoma before first-line chemotherapy, no disease progression (i.e., ongoing complete response, partial response, or stable disease) after receiving 4 to 6 cycles of chemotherapy with gemcitabine and either cisplatin or carboplatin, and a treatment-free interval of 4-10 weeks since the last dose of chemotherapy. A total of 700 patients were randomized (1:1) to receive to maintenance therapy with avelumab 10 mg/kg intravenously every 2 weeks (N=350) plus BSC or BSC alone (N=350) until disease progression or unacceptable toxicity. The primary endpoint was OS in 2 primary populations: all randomized patients and patients with PD-L1+ tumors. Secondary endpoints included progression-free survival (PFS) and safety. Avelumab significantly prolonged OS in all randomized patients (hazard ratio [HR] 0.69; 95% CI, 0.56, 0.86; 1-sided P<0.001) and in the PD-L1+ population (HR 0.56; 95% CI, 0.40, 0.79; 1-sided P<0.001). Median OS was 21.4 with avelumab vs 14.3 months with BSC alone in all randomized patients and not reached with avelumab vs 17.1 months with BSC alone in patients with PD-L1+ tumors.

All-cause adverse events of any grade occurred in 98.0% of patients in the avelumab plus best supportive care arm and 77.7% of patients in the best supportive care alone arm, including grade ≥3 events in 47.4% and 25.2%, respectively. No new safety signals were identified and maintenance avelumab had a low rate of treatment discontinuation due to adverse events (11.9%).

We greatly appreciate the Panel's thorough consideration of the data for avelumab as a first-line maintenance therapy for patients with locally advanced or metastatic bladder cancer (Stage IV) whose disease has not progressed with platinum-based induction chemotherapy.

Best regards,

Constantin and Kirk

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