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NCCN Guidelines Panel:	Bladder Cancer

Dear NCCN Bladder Cancer Panel and Members:

This letter is a formal request to the National Comprehensive Cancer Network (NCCN) Panel for inclusion of IMFINZI™ (durvalumab) in the treatment of locally advanced or metastatic urothelial carcinoma. IMFINZI is a programmed death-ligand 1 (PD-L1) blocking antibody.

Specific Changes: Request inclusion of IMFINZI™ (durvalumab) on BL-G2 of 4 as a standard regimen under “Subsequent systemic therapy for locally advanced or metastatic disease”.

FDA Status: IMFINZI was approved by FDA on May 1, 2017 for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:

- have disease progression during or following platinum-containing chemotherapy.
- have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Please refer to the [IMFINZI](#) prescribing information for the full FDA-approved indication and safety information.

Rationale: The FDA based its approval of IMFINZI on results from Study 1108 trial. Background and results from the studies are as follows:

- This multicenter, multi-cohort, Phase I/II trial evaluated the efficacy and safety of IMFINZI 10 mg/kg given intravenously every 2 weeks in 182 patients with locally advanced or metastatic urothelial carcinoma. FDA approval was based on patients in the urothelial carcinoma cohort who were previously treated with platinum-containing chemotherapy.¹
- IMFINZI demonstrated the following clinical activity: a confirmed objective response rate (ORR) of 17.0%, complete response (CR) of 2.7%, and partial response (PR) of 14.3% for all patients, and ORR of 26.3%, CR of 3.2%, and PR of 23.2% in patients who had high PD-L1 expression. Median follow-up time was 5.6 months. Median duration of response had not been reached in the overall population.¹
- For adverse reactions in urothelial carcinoma patients treated with durvalumab at 10 mg/kg every 2 weeks, the most common Grade 3 or 4 adverse events (≥3%) were fatigue, urinary tract infection, musculoskeletal pain, abdominal pain, dehydration, and general physical health deterioration. Serious adverse events occurred in 46.0% of patients. The most frequent serious adverse events (>2%) were acute kidney injury (4.9%), urinary tract infection (4.4%), musculoskeletal pain (4.4%), liver injury (3.3%),

general physical health deterioration (3.3%), sepsis, abdominal pain, pyrexia/tumor associated fever (2.7% each).¹

- IMFINZI is approved with a complementary diagnostic (Ventana PD-L1 [SP263] Assay) by Ventana Medical Systems Inc. (a member of the Roche Group)³.
- Additional data (which includes median overall survival (OS) of 14.1 months in patients with locally advanced or metastatic urothelial carcinoma who had progressed on prior chemotherapy) at the October 24, 2016 data cut-off was presented at the American Society of Clinical Oncology, Genitourinary Cancer Symposium (ASCO-GU) and is being provided for your review.²

These materials may include information that is not found in the currently approved prescribing information for IMFINZI. The enclosed information is intended to provide pertinent data and should in no way be construed as a recommendation for the use of this product in any manner other than as approved by the Food and Drug Administration and as described in the prescribing information for IMFINZI. This information is provided to NCCN evaluators for guideline review purposes only.

Data Sources: The following references are submitted in support of this proposal.

1. IMFINZI™ (durvalumab) Prescribing Information
2. Powles T, O'Donnell PH, Massard C, et. al. Updated Efficacy and Tolerability of Durvalumab in Locally Advanced or Metastatic Urothelial Carcinoma. Presented at American Society of Clinical Oncology-Genitourinary Cancers Symposium (ASCO GU) 2017; Orlando, FL; February 16-18, 2017; Poster No. 286
3. Ventana PD-L1 (SP263) Assay Package Insert

Sincerely,

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