Dear NCCN NSCLC 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 NCCN Guidelines for treatment of metastatic NSCLC in patients who have progressed after one or more systemic treatment, based on the enclosed data. IMFINZI is a programmed death-ligand 1 (PD-L1) blocking antibody.

**Specific Change:** We request inclusion of IMFINZI on the algorithm presented on page NSCL-24.

**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.¹

Please refer to the IMFINZI prescribing information for the full FDA-approved indication and safety information.

- IMFINZI is not FDA-approved for use in patients with NSCLC.

**Rationale:**
1. The clinical evidence from a large Phase II (Study 1108), multicenter, open-label study for the NSCLC expansion cohort was presented at European Society of Medical Oncology; October 7-11, 2016.²
   - Three-hundred four patients with advanced NSCLC received durvalumab 10 mg/kg every 2 weeks; A total of 287 patients were evaluable for response (defined as patients who had received any dose of durvalumab, with measurable disease at baseline, and ≥1 on-study scan or who discontinued due to disease progression or death prior to first on-study scan) (data cut-off April 29, 2016)
   - Clinical activity with durvalumab was observed in both squamous and non-squamous advanced NSCLC, as well as in both treatment-naïve and previously treated patients with advanced NSCLC
     - Durvalumab as 1st line treatment:
       - ORR: 28.6% (high PD-L1 expression) and 11.1% (low PD-L1 expression)
       - Median OS: 17.1 months (high PD-L1 expression) and 7.4 months (low PD-L1 expression)
     - Durvalumab as 2nd line treatment:
       - ORR: 26.1% (high PD-L1 expression) and 4.2% (low PD-L1 expression)
       - Median OS: 17.8 months (high PD-L1 expression) and 8.2 months (low PD-L1 expression)
     - Durvalumab as ≥3rd line treatment:
• ORR: 22.0% (high PD-L1 expression) and 6.1% (low PD-L1 expression)
• Median OS: 13.0 months (high PD-L1 expression) and 7.6 months (low PD-L1 expression)

Safety Highlights in the Treated Population (n=304):
  o Most common AEs include fatigue, decreased appetite, and diarrhea
  o Drug-related AEs led to discontinuation in 5.3% of patients
  o There was 1 drug-related death reported due to pneumonia
  o Grade ≥3 drug-related AEs were reported in 10.2% of patients

2. The clinical evidence from a Phase II (ATLANTIC) open-label, single-arm trial of durvalumab specifically in patients with EGFR/ALK wild-type NSCLC who received at least 2 prior systemic treatment regimens, including 1 platinum-based chemotherapy regimen. This data was presented at the World Congress on Lung Cancer, December 6, 2016.³
• Patients were treated with durvalumab monotherapy 10 mg/kg intravenous (IV) every 2 weeks for up to 12 months
• In Cohort 2, the objective response rate (ORR) was 16.4% in (PD-L1) high group (n=146 patients evaluable for response) and 7.5% in the PD-L1 low/negative group (n=93 patients evaluable for response). Overall survival (OS) at 1 year was 47.7% in patients with PD-L1 high tumors (n=149), and 34.5% in patients with PD-L1 low/negative tumors (n=94)
• In Cohort 2, treatment-related Grade ≥3 adverse events (AEs) were reported in 8.3% of patients, treatment-related AEs leading to discontinuation were reported in 3% of patients, and immune-mediated AEs were reported in 10.2% of patients

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 and to assist in your review.

1. IMFINZI™ (durvalumab) Prescribing Information

Sincerely,

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