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Submitted by:
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Date of request: April 17, 2017
NCCN Guidelines Panel: Bladder Cancer

On behalf of Genentech, Inc., I respectfully request the NCCN Bladder Cancer Guideline Panel to review the enclosed data for:

- **Tecentriq® (atezolizumab)**

  Balar AV, Galsky MD, Rosenberg JE, et al. Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: a single-arm, multicentre, phase 2 trial. Lancet 2017;389: 67-76.
  https://www.ncbi.nlm.nih.gov/pubmed/?term=27939400

Specific Changes:
Please consider the recent Food and Drug Administration (FDA) approval to support the inclusion of Tecentriq in the treatment of cisplatin-ineligible patients with locally advanced or metastatic urothelial carcinoma.

FDA Clearance:
Tecentriq was approved by the FDA on April 17, 2017 for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy. Tecentriq is also FDA-approved in patients who have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant 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 Tecentriq prescribing information for the full FDA-approved indications and safety information. http://www.gene.com/download/pdf/tecentriq_prescribing.pdf

Rationale:
The FDA approval of Tecentriq was based on the results of Cohort 1 of the single-arm, Phase II IMvigor 210 trial.[1] This cohort contained 119 patients with locally advanced or metastatic urothelial carcinoma ineligible for cisplatin-containing chemotherapy and were either previously untreated or had disease progression at least 12 months after neoadjuvant or adjuvant chemotherapy. The primary endpoint was overall response rate (ORR). Secondary endpoints included overall survival (OS), progression-free survival (PFS), and duration of response (DOR).

The US prescribing information (USPI) and the oral presentation from the American Society of Clinical Oncology (ASCO) 2016 Annual Meeting both report results with a median follow-up of 14.4 months, while the full publication reports follow-up of 17.2 months[1,2] The IMvigor 210 Cohort 1 oral presentation and full publication were previously submitted.

Efficacy[1,2]:

- The following table reflects efficacy results from the USPI:

Efficacy Outcomes in IMvigor 210 – Cohort 1[1]			
	All Patients	**PD-L1 Expression Subgroups**	
	N=119	**PD-L1 Expression of < 5% in ICs (N=87)**	**PD-L1 Expression of ≥ 5% in ICs (N=32)**
Number of IRF-assessed Confirmed Responders	28	19	9
ORR % (95% CI)	23.5% (16.2-32.2)	21.8% (13.7-32.0)	28.1% (13.8-46.8)
Complete Response (CR) (%)	6.7%	6.9%	6.3%
Partial Response (PR) (%)	16.8%	14.9%	21.9%
Median DoR, months (range)	NR (3.7-16.6+)	NR (3.7-16.6+)	NR (8.1-15.6+)
+ Denotes a censored value Abbreviations: CI=confidence interval; DoR=duration of response; IC=tumor-infiltrating immune cell; IRF=independent review facility; ORR=objective response rate; NR=not reached; PD-L1=programmed death-ligand 1			

- In 24 patients with disease progression following neoadjuvant or adjuvant therapy, the ORR was 33.0% (95% CI: 16%-55%).[1] This pre-specified analysis resulted in the inclusion of these patients as part of the FDA-approved patient population.
- Secondary endpoints were reported in the full publication.[2]

Safety[1]:

- The most common Grade 3–4 adverse reactions (≥ 2%) were fatigue, urinary tract infection, anemia, diarrhea, blood creatinine increase, intestinal obstruction, ALT increase, hyponatremia, decreased appetite, sepsis, back/neck pain, renal failure, and hypotension.
- Tecentriq was discontinued for adverse events in 4.2% of patients. The USPI reports a different discontinuation rate for Tecentriq than the full publication because it does not include deaths as a reason for discontinuation.

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I hope this information is helpful to you. If you have any questions, please contact me directly at (650) 467-0637 or by email at yang.ellen@gene.com.

Respectfully submitted,

Ellen Yang

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Supplemental References:

1. Tecentriq® [package insert]. Genentech; South San Francisco, CA. 2017.
2. Balar AV, Galsky MD, Rosenberg JE, et al. Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: a single-arm, multicentre, phase 2 trial. Lancet 2017;389:67-76.

C#17-M0041

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