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Date of request: August 23, 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):**

  Powles T, Loriot Y, Durán I, et al. IMvigor211: a Phase III randomized study examining atezolizumab vs. chemotherapy for platinum-treated advanced urothelial carcinoma. Presented at the 2nd Special Conference of the EACR-AACR-SIC in Florence, Italy; 2017 Jun 24-27. EACR AACR SIC Oral Presentation .

FDA Clearance:[1]
Tecentriq is approved by the Food and Drug Administration (FDA) for the treatment of patients with:

- locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy, or
- locally advanced or metastatic urothelial carcinoma who received prior platinum chemotherapy.

These indications are still approved under accelerated approval based on tumor response rate and duration of response. In addition, Tecentriq is FDA-approved for patients with metastatic non-small cell lung cancer who have disease progression during or following platinum-containing chemotherapy.

Please refer to the Tecentriq prescribing information for the full FDA-approved indication and safety information. http://www.gene.com/download/pdf/tecentriq_prescribing.pdf

Rationale:
The Phase 3 IMvigor211 trial was a multicenter, open-label, randomized study that assessed the efficacy and safety of Tecentriq compared to chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer.[2,3] A total of 931 patients were randomized to either Tecentriq 1,200 mg intravenous (IV) every 3 weeks or investigator's choice of chemotherapy (vinflunine, paclitaxel, or docetaxel) every 3 weeks. The primary endpoint was overall survival (OS), while secondary endpoints included overall response rate (ORR), progression-free survival (PFS), duration of response (DOR), and safety. The median follow-up in the intent-to-treat (ITT) population was 17.3 months (range, 0-24.5).

Efficacy Outcomes in IMvigor211[3]*						
Efficacy Endpoint	**PD-L1 IC2/3**		**PD-L1 IC1/2/3**		**ITT**	
	Tecentriq	**CT**	**Tecentriq**	**CT**	**Tecentriq**	**CT**
Overall Survival						
	n=116	n=118	n=316	n=309	n=467	n=464
Median, mo (95% CI)	11.1 (8.6-15.5)	10.6 (8.4-12.2)	8.9 (8.2-10.9)	8.2 (7.4-9.5)	8.6 (7.8-9.6)	8.0 (7.2-8.6)
	HR=0.87; p=0.41		HR=0.87; p=0.14		HR=0.85; p=0.038	
Confirmed Response Rates per RECIST v1.1[†]						
	n=113	n=116	n=312	n=306	n=462	n=461
ORR[†], % (95% CI)	23 (16-32)	22 (15-30)	14 (10-19)	15 (11-19)	13 (11-17)	13 (11-17)
mDoR, mo (95% CI)	NR	NR	NR	NR	21.7 (13.0-21.7)	7.4 (6.1-10.3)

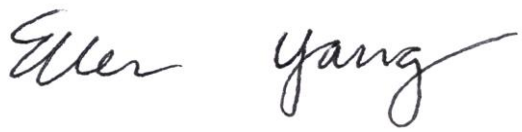
* Data cutoff: March 13, 2017. [†] Confirmed response was not required for secondary efficacy endpoints. These confirmed responses were assessed as an exploratory endpoint.
Abbreviations: CI=confidence interval; CR=complete response; CT=chemotherapy; mDoR=median duration of response; HR=hazard ratio; IC=tumor-infiltrating immune cell; ITT=intent-to-treat; NR=not reported; ORR=objective response rate; PD-L1=programmed death-ligand 1; RECIST=Response Evaluation Criteria in Solid Tumors.

Progression-free survival has not yet been reported. At the time of data cutoff, there were ongoing responses in 63% of responders in the Tecentriq arm and 21% of responders in the chemotherapy arm. As a pre-specified subgroup endpoint based on chemotherapy type, median overall survival was improved in patients treated with Tecentriq, 8.3 months (95% CI: 6.6-9.8), vs taxanes, 7.5 months (95% CI: 6.7-8.6), HR=0.73 (95% CI: 0.58-0.92).

Treatment-related all-grade adverse events were reported in 70% of Tecentriq-treated patients (N=459) and in 89% of chemotherapy-treated patients (N=443); 20% vs 43% were of Grade 3-4 and 1% vs 2% were of Grade 5 severity.[3] Treatment-related serious adverse events were reported in 16% of Tecentriq-treated patients and in 25% of chemotherapy-treated patients. Three percent of patients in the Tecentriq arm experienced a treatment-related adverse event leading to treatment discontinuation compared with 14% in the chemotherapy arm.

Additional data have been reported on the use of Tecentriq in patients with locally advanced or metastatic urothelial carcinoma previously treated with platinum chemotherapy.[4] Any references supplied to you are protected under U. S. Copyright Law (Title 17, U.S. Code). No further reproduction is permitted. 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,



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Supplemental References:

1. Tecentriq® [package insert]. Genentech; South San Francisco, CA. 2017.
2. Hoffmann-La Roche. A study of atezolizumab compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer [IMvigor211]. August 2017. Available at https://clinicaltrials.gov/ct2/show/NCT02302807. Accessed on August 15, 2017.
3. Powles T, Loriot Y, Durán I, et al. IMvigor211: a Phase III randomized study examining atezolizumab vs. chemotherapy for platinum-treated advanced urothelial carcinoma. Presented at the 2nd Special Conference of the EACR-AACR-SIC in Florence, Italy; June 24–27, 2017. EACR AACR SIC Oral Presentation.
4. Rosenberg JE, Hoffman-Censits J, Powles T, et al. Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with

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platinum-based chemotherapy: a single-arm, multicentre, Phase 2 trial. Lancet 2016;387:1909-1920. https://www.ncbi.nlm.nih.gov/pubmed/26952546

C#17-M0107

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