CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
3Q17 July-August

**BRAND NAME**
Tecentriq®

**GENERIC NAME**
atezolizumab

**MANUFACTURER**
Genentech

**DATE OF APPROVAL**
April 17, 2017

**PRODUCT LAUNCH DATE**
April 17, 2017

**REVIEW TYPE**

☐ Review type 1 (RT1): New Drug Review
*Full review of new chemical or biologic agents*

☐ Review type 2 (RT2): New Indication Review
*Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use*

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
*Expedited abbreviated review of Centers for Medicare & Medicaid Services (CMS) protected class drugs (anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants)*

☒ Review type 5 (RT5): Abbreviated Reviews for Intravenous Chemotherapy Agents
*Abbreviated review for intravenous chemotherapy agents which are usually covered under the medical benefit*

**FDA APPROVED INDICATIONS**
Current Indication(s):
Tecentriq has been indicated for:

- The treatment of patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy;
- The treatment of patients with metastatic non-small cell lung cancer (NSCLC) who have disease progression during or following platinum-containing chemotherapy. Patients with

EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Tecentriq.

New Indication(s):
Treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.

**OFF-LABEL USES**
Not applicable

**CLINICAL EFFICACY[1]**
The efficacy of Tecentriq as first line therapy for locally advanced or mUC in patients who are ineligible for cisplatin therapy was established in a phase 2 multicenter, single-arm study of 119 patients who were either previously untreated or had disease progression at least 12 months after neoadjuvant or adjuvant chemotherapy. All patients were given Tecentriq 1200 mg intravenously every 21 days until disease progression.

Patients were required to be cisplatin-ineligible per one or more of the following: glomerular filtration rate >30 mL/min and <60 mL/min (Cockcroft-Gault formula), grade 2 or higher hearing loss or peripheral neuropathy, or an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 2.

The primary endpoint was the objective response rate (ORR), assessed in pre-specified subgroups based on PD-L1 expression and in all patients. Secondary endpoints included duration of response, progression-free survival and overall survival.

| | 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) |
| ORR (95% CI) | 23% (16-31) | 22% (14-32) | 28% (14-47) |
| Duration of response, months (95% CI) | NR (3.7-NE) | NR (3.7-NE) | NR (8.1-NE) |
| Progression-free, months (95% CI) | 2.7 (2.1-4.2) | N/A | 4.1 (2.3-11.8) |
| Overall survival, months (95% CI) | 15.9 (10.4-NE) | 19.1 (9.8-NE) | 12.3 (6.0-NE) |

IC=tumor-infiltrating immune cell; NR=not reached; NE=not estimable; N/A=not applicable (not reported)

Seventy-seven patients (64.7%) discontinued treatment due to disease progression.

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**CONTRAINDICATIONS**
Not applicable

**BLACK BOX WARNINGS**
Not applicable

**DRUG INTERACTIONS**
Not applicable

**ADVERSE REACTIONS**
In cisplatin-ineligible patients with locally advanced or mUC, the most common adverse reactions (≥ 20%) were fatigue (52%), decreased appetite (24%), diarrhea (24%), and nausea (22%). 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.

In previously treated patients with locally advanced or mUC, the most common adverse reactions (≥ 20%) were fatigue (52%), decreased appetite (26%), nausea (25%), urinary tract infection (22%), pyrexia (21%), and constipation (21%). The most common Grade 3–4 adverse reactions (≥ 2%) were urinary tract infection, anemia, fatigue, dehydration, intestinal obstruction, urinary obstruction, hematuria, dyspnea, acute kidney injury, abdominal pain, venous thromboembolism, sepsis, and pneumonia.

Across three pivotal trials for mUC and NSCLC, 41.5%-54.1% of patients tested positive for treatment-emergent (treatment-induced or treatment-enhanced) anti-therapeutic antibodies (ATA) at one or more post-dose time points. In these studies, the presence of ATAs did not appear to have a clinically significant impact on pharmacokinetics, safety or efficacy.

**DOSAGE AND ADMINISTRATION**
The recommended dose of Tecentriq for all indications is 1200 mg administered as an intravenous infusion over 60 minutes every 3 weeks until disease progression or unacceptable toxicity.

**PRODUCT AVAILABILITY**
Single dose vial: 1200 mg/20 mL (60 mg/mL)

**THERAPEUTIC ALTERNATIVES**

| DRUG NAME | USAGE REGIMEN (route of admin/frequency of use) | COMMENTS |
|---|---|---|
| **cisplatin** | **mUC** | |

| | | |
|---|---|---|
| | GC (every 21 days for 2 to 4 cycles): gemcitabine 1,000 mg/m2 days 1, 8 and 15; cisplatin 70 mg/m2 day 2<br>or<br>DD-MVAC (every 14 days for 4 or more cycles until disease progression or unacceptable toxicity):<br>Methotrexate IV push on day 1<br>Vinblastine IV push on day 2<br>Doxorubicin IV push on day 2<br>Cisplatin IV infusion on day 2 | |
| **carboplatin** | **mUC**<br>gemcitabine 1,000 mg/m$^2$ on days 1 and 8, and carboplatin on day 1, every 21 days | Off-label usage for mUC, but supported by NCCN for cisplatin-ineligible patients.[2] |

**Boldface indicates generic availability**

| **Utilization Management Recommendation** |
|---|
| • There is not significant potential for inappropriate use.<br>• Requiring utilization management (e.g., prior authorization) to prevent off-label usage would be clinically appropriate. |
| Product Comparison |
| • It would not be clinically appropriate to require a trial of platinum-based chemotherapy prior to initiation of Tecentriq for patients with locally advanced or metastatic urothelial carcinoma who are cisplatin-ineligible.<br>• It would be clinically appropriate to require a trial of platinum-based chemotherapy for patients with locally advanced or metastatic urothelial carcinoma who are cisplatin-eligible. |

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REFERENCES

[1] Tecentriq [Prescribing Information]. South San Francisco, CA: Genentech, Inc.; April 2017.
[2] Bladder cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed April 2017.