CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
3Q17 July – August

BRAND NAME
Bavencio®

GENERIC NAME
Avelumab

MANUFACTURER
EMD Serono, Inc.

DATE OF APPROVAL
May 9, 2017

PRODUCT LAUNCH DATE
Currently commercially available

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 protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

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

FDA APPROVED INDICATION(S)
Previously Existing Indication
Bavencio is indicated for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC).

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

New Indication
Bavencio is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) 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 and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

OFF-LABEL USES
As a single agent for urothelial carcinoma recurrence post cystectomy (per National Comprehensive Cancer Network Drugs and Biologics Compendium).

CLINICAL EFFICACY[1]
The efficacy and safety of Bavencio was demonstrated in the UC cohorts of the JAVELIN Solid Tumor trial, an open-label, single-arm, multi-center study that included 242 patients with locally advanced or metastatic UC with disease progression on or after platinum-containing chemotherapy or who had disease progression within 12 months of treatment with a platinum-containing neoadjuvant or adjuvant chemotherapy regimen. Patients received Bavencio at a dose of 10 mg/kg intravenously every 2 weeks until radiographic or clinical progression or unacceptable toxicity.

Efficacy outcome measures included confirmed overall response rate (ORR), as assessed by an Independent Endpoint Review Committee (IERC) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, and duration of response. Efficacy was evaluated in patients who were followed for a minimum of both 13 weeks and 6 months at the time of data cut-off. Confirmed ORR in patients who had been followed for at least 13 weeks was 13.3% (n=30) (95% CI: 9.1, 18.4), and 16.1% (n=26) (95% CI: 10.8, 22.8) in patients who had been followed for at least 6 months. Median time to response was 2.0 months (range 1.3-11.0) among patients followed for either ≥ 13 weeks or ≥ 6 months. The median response duration had not been reached in patients followed for at least 13 weeks or at least 6 months, but ranged from 1.4+ to 17.4+ months in both groups.

Efficacy Endpoints	**≥ 13 Weeks Follow-Up (N=226)**	**≥ 6 Months Follow-Up (N=161)**

Confirmed Overall Response Rate		
Overall Response Rate n (%)	30 (13.3%)	26 (16.1%)
(95% CI)	(9.1, 18.4)	(10.8, 22.8)
Complete Response n (%)	9 (4.0%)	9 (5.6%)
Partial Response n (%)	21 (9.3%)	17 (10.6%)
Duration of Response		
Median, months (range)	NE (1.4+ to 17.4+)	NE (1.4+ to 17.4+)

CI: Confidence interval; NE: Not estimable; + denotes a censored value

CONTRAINDICATIONS
Not applicable

BLACK BOX WARNINGS
Not applicable

DRUG INTERACTIONS
Not applicable

ADVERSE REACTIONS
Most common adverse reactions (≥ 20%) in patients with locally advanced or metastatic urothelial carcinoma were fatigue, infusion-related reaction, musculoskeletal pain, nausea, decreased appetite, and urinary tract infection.

DOSAGE AND ADMINISTRATION
The recommended dose of Bavencio is 10 mg/kg administered as an intravenous (IV) infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity.

Patients should be pre-medicated with an antihistamine and with acetaminophen prior to the first 4 infusions of Bavencio. Premedication should be administered for subsequent Bavencio doses based upon clinical judgment and presence/severity of prior infusion reactions.

PRODUCT AVAILABILITY
Injection: 200 mg/10 mL (20 mg/mL) solution in single-dose vial.

THERAPEUTIC ALTERNATIVES

DRUG NAME	USAGE REGIMEN[2,3,4,5] (route of admin/frequency of use)	COMMENTS
atezolizumab (Tecentriq®)	UC[6] 1200 mg administered as an IV infusion over 60 minutes every 3 weeks until	

	disease progression or unacceptable toxicity	
durvalumab (Imfinzi™)	UC 10 mg/kg as an IV infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity	
nivolumab (Opdivo®)	UC 240 mg IV infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity	
pembrolizumab (Keytruda®)	UC 200 mg IV infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression	

Boldface indicates generic availability

Utilization Management Recommendation
• There is significant potential for inappropriate use and utilization management should be considered for the following reason(s): o To ensure appropriate use of medications that have a significant potential for use that may lead to inferior or unpredictable outcome: i. Bavencio is a second-line systemic therapy option after platinum-based therapy for locally advanced or metastatic urothelial carcinoma. ii. Recommended utilization management tool(s): (check all that apply) (1) ☒ Prior authorization (2) ☐ Quantity limits (3) ☐ Provider newsletter (4) ☐ Hard block (plan exclusion) (5) ☐ Messaging (6) ☐ Electronic step therapy (7) ☐ Clinical program
Product Comparison
• Not applicable

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[1] Bavencio Prescribing Information. Rockland, MA: EMD Serono, Inc.; May 2017. Available at: https://www.bavencio.com/. Accessed May 19, 2017.
[2] Tecentriq Prescribing Information. South San Francisco, CA: Genentech, Inc.; April 2017. Available at https://www.tecentriq.com/. Accessed May 19, 2017.
[3] Imfinzi Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; May 2017. Available at https://www.imfinzi.com/. Accessed May 19, 2017.
[4] Opdivo Prescribing Information. Princeton, NJ: Bristol-Myers Squibb; April 2017. Available at http://www.opdivo.com/. Accessed May 19, 2017.
[5] Keytruda Prescribing Information. Whitehouse Station, NJ: Merck Sharp &Dohme Corp.; May 2017. Available at: http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf. Accessed May 19, 2017.