STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Bavencio (avelumab)
PAM–026

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	10/20/2017
Revision Number:	5	**Last Rev Date:**	10/20/2023
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	10/18/2024
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	11/27/2017

Overview

Medication:[1]	avelumab
Brand Name:	Bavencio®
Pharmacologic Category:	Programmed death ligand-1 (pd-L1) blocking antibody (immune checkpoint inhibitor)

FDA-Approved Indication(s):	• Merkel Cell Carcinoma (MCC): Adults and pediatric patients 12 years and older with metastatic MCC
	• Urothelial Carcinoma (UC):
	  ○ Maintenance treatment of patients with locally advanced or metastatic UC that has not progressed with first-line platinum-containing chemotherapy
	  ○ Patients with locally advanced or metastatic UC (mUC) who have:
	  ▪ Disease progression during or following platinum-containing chemotherapy
	  ▪ Disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing therapy
	• Renal Cell Carcinoma (RCC): First-line treatment, in combination with axitinib, of patients with advanced RCC

How Supplied:	Single-dose vial containing 200 mg/10 mL (20 mg/mL) of avelumab
Dosage and Administration:	Administer via intravenous (IV) infusion: • MCC: 800 mg every 2 weeks until disease progression or unacceptable toxicity • UC: 800 mg every 2 weeks until disease progression or unacceptable toxicity • RCC: 800 mg every 2 weeks [in combination with axitinib (Inlyta®) 5 mg orally twice daily] until disease progression or unacceptable toxicity
Benefit Category:	Medical

Descriptive Narrative

Merkel cell carcinoma (MCC) is a rare, aggressive, cutaneous malignancy has a high propensity for recurrence and metastases. Patients typically present with a rapidly growing, painless, firm, nontender, shiny, flesh-colored or bluish-red, intracutaneous nodule commonly located in the head and neck region. MCC is often clinically misdiagnosed as a benign lesion (e.g., cyst, lipoma, pyogenic granuloma). Recognized risk factors for MCC include light skin color, increasing age, male sex, immunosuppression, and other malignancies.

Data from the Surveillance, Epidemiology, and End Results (SEER) Program database indicate that in the United States, the estimated annual incidence rate rose from 0.5 cases per 100,000 persons in 2000 to 0.7 cases per 100,000 persons in 2013. MCC incidence increases exponentially with advancing age, from 0.1 to 1 to 9.8 (per 100,000 person-years) among age groups 40 to 44, 60 to 64, and > 85 years, respectively. Due to aging of the population, the United States' MCC incidence is predicted to climb to more than 3200 cases in 2025.[2]

Bladder cancer is the most common malignancy involving the urinary system. Urothelial (transitional cell) carcinoma is the predominant histologic type in the United States.[3] In 2023, the United States is expected to see 82,290 new cases of bladder cancer with an estimated 16,710 deaths.[4] About 90 percent of patients with bladder cancer are over the age of 55 years, with an average age of 73 years at the time of diagnosis. Overall, the chance that men will develop this cancer in their lifetime is about 1 in 28 men. For women, the chance is about 1 in 91. Urothelial cancer is strongly associated with smoking and increased dietary fat. Because these are also factors that predispose to other medical conditions, including cardiovascular, cerebrovascular, and pulmonary disease, patients with urothelial cancer often have significant comorbidities.[5]

Renal cell carcinomas (RCCs), which originate within the renal cortex, are responsible for 80 to 85 percent of all primary renal neoplasms. In the United States, there are approximately 82,000 new cases and almost 15,000 deaths from RCC each year. RCC occurs predominantly in the sixth to eighth decade of life, with median age at diagnosis of 64 years. RCC is approximately twofold more common in males compared with females.

Established risk factors for development of renal cell carcinoma include cigarette smoking, hypertension, obesity, acquired cystic disease of the kidney and chronic kidney disease, genetic factors, chronic hepatitis C infection, sickle cell disease, and kidney stones. Occupational exposure (i.e., exposure to toxic compounds), prolonged, heavy ingestion of analgesics, and the use of cytotoxic chemotherapy are also considered established risk factors.[6]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[7]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for Merkel Cell Carcinoma (Version 1.2023 – April 10, 2023).[8]
- NCCN Guidelines® for Bladder Cancer (Version 3.2023 – May 25, 2023).[9]
- NCCN Guidelines® for Kidney Cancer (Version 1.2024 – June 21, 2023).[10]

NCCN Guidelines® Recommendation(s) for avelumab (Bavencio®) in Merkel Cell Carcinoma
(1) Disseminated disease M1: Preferred interventions: Avelumab: Category 2A [a]
[a] Data from non-randomized trials in patients with MCC demonstrate that rates of durable response are improved with PD-1/PD-L1 blockade compared with cytotoxic therapy. The safety profiles for checkpoint immunotherapies are significantly different from cytotoxic therapies. Consult prescribing information for recommendations on detection and management of immune-related adverse events associated with checkpoint immunotherapies. Clinician and patient education is critical for safe administration of checkpoint immunotherapies.

NCCN Guidelines® Recommendation(s) for avelumab (Bavencio®) in Bladder Cancer
(1) First-line systemic therapy for locally advanced or metastatic disease (Stage IV) A. Cisplatin eligible, preferred regimens i. Gemcitabine and cisplatin (category 1) followed by avelumab maintenance therapy (category 1) [b] ii. ddMVAC w/ growth factor support (category 1) followed by avelumab maintenance therapy (cat. 1) [b] B. Cisplatin ineligible, preferred regimens i. Gemcitabine and carboplatin (category 1) followed by avelumab maintenance therapy (category 1) [b]
(2) Second-line systemic therapy for locally advanced or metastatic disease (Stage IV) (post-platinum or other chemotherapy) [c,d] A. Alternative preferred regimens i. Immune checkpoint inhibitor: avelumab: Category 2A
ddMVAC = dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin
[b] Maintenance therapy with avelumab only if there is no progression on first-line platinum-containing chemotherapy.
[c] Participation in clinical trials of new agents is recommended.
[d] If progression-free survival >12 months after platinum (e.g., cisplatin or carboplatin), consider re-treatment with platinum if the patient is still platinum eligible.

NCCN Guidelines® Recommendation(s) for avelumab (Bavencio®) in Kidney Cancer
(1) First-line therapy for clear cell histology [e] i. Favorable risk: Axitinib + avelumab: Category 2A, other recommended regimen i. Poor/intermediate risk: Axitinib + avelumab: Category 2A, other recommended regimen
(2) Subsequent therapy for clear cell histology [f] i. IO therapy naïve: Axitinib + avelumab: Category 3, useful in certain circumstances [g] i. Prior IO therapy: Axitinib + avelumab: Category 3, useful in certain circumstances [g]
[e] Divided according to risk, from *Risk Models to Direct Treatment* [Memorial Sloan Kettering Cancer Center (MSKCC) Prognostic Model]
[f] Divided according to Immuno-oncology (IO) Therapy History Status
g **NOTE:** Category 3 indicates that based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate. Therapy listed here for informational purposes only.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale[11]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

GRADE	ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score]
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.
5	Dead.

Criteria

Prior authorization is required.

Merkel Cell Carcinoma (MCC) – Initial Approval Criteria

Bavencio® (avelumab) is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of metastatic Merkel cell carcinoma (MCC); **AND**
2. Member is 12 years of age or older; **AND**
3. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
4. Member does not have active or history of an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant; **AND**
5. Member has not had a prior organ or allogeneic stem cell transplant; **AND**
6. Member has not been previously treated with anti-PD-1 (programmed death receptor-1), anti-PD-L1 (programmed death ligand-1), or anti-CTLA-4 (cytotoxic T-lymphocyte antigen 4) antibodies; **AND**
7. Member does not have active or history of central nervous system (CNS) metastases; **AND**
8. Member does not have significant acute or chronic infection; **AND**
9. Member has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; **AND**
10. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 800 mg every 2 weeks; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Urothelial Carcinoma (UC) – Initial Approval Criteria

Bavencio® (avelumab) is considered medically when **ALL** of the following are met:

1. Diagnosis of recurrent, advanced, or metastatic urothelial carcinoma (UC); **AND**
2. Member has received prior treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin) and meets **ONE** of the following criteria:
    a. Is using Bavencio® as subsequent therapy after disease progression during or following the platinum-containing regimen; **OR**
    b. Is using Bavencio® as maintenance therapy following completion of the platinum-containing regimen with no evidence of disease progression; **OR**
    c. Has confirmed disease progression within 12 months of receiving neoadjuvant or adjuvant treatment with platinum-containing regimen; **AND**
3. Member is 18 years of age or older; **AND**
4. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
5. Member does not have an active or history of an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant; **AND**
6. Member has not had a prior organ or allogeneic stem cell transplant; **AND**
7. Member has not been previously treated with anti-PD-1 (programmed death receptor-1), anti-PD-L1 (programmed death ligand-1), or anti-CTLA-4 (cytotoxic T-lymphocyte antigen 4) antibodies; **AND**
8. Member does not have active or history of central nervous system metastases; **AND**
9. Member does not have significant acute or chronic infection; **AND**
10. Member has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; **AND**
11. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 800 mg every 2 weeks; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Renal Cell Carcinoma (RCC) – Initial Approval Criteria

Bavencio® (avelumab) is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of advanced renal cell carcinoma (RCC) (histological confirmation with clear cell component); **AND**
2. Member is 18 years of age or older; **AND**
3. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
4. Member does not have active or history of an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant; **AND**
5. Member does not have newly diagnosed or active brain metastasis; **AND**
6. Member is using as first-line therapy in combination with axitinib (Inlyta®); **AND**
7. Member has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; **AND**

8. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 800 mg every 2 weeks; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Continuation Criteria (all above indications)

Bavencio® (avelumab) is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 800 mg every 2 weeks (until disease progression or unacceptable toxicity); or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	800 mg every 2 weeks	800 mg every 2 weeks until disease progression or unacceptable toxicity

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9023	Injection, avelumab, 10 mg

ICD-10	Description
C4A.0 – C4A.9	Merkel cell carcinoma
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1, C65.2, C65.9	Malignant neoplasm of renal pelvis
C66.1, C66.2, C66.9	Malignant neoplasm of ureter
C67.0 – C67.9	Malignant neoplasm of bladder
C68.0	Malignant neoplasm of urethra

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
44087-3535-01	EMD Serono, Inc.	10 mg	1	EA	20

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Bavencio® prescribing information (09/2023). EMD Serono, Inc.: Rockland, MA. Available online at: www.bavencio.com/hcp. Accessed October 9, 2023.

[2] Tai P, Nghiem PT, Park SY. Pathogenesis, clinical features, and diagnosis of Merkel cell (neuroendocrine) carcinoma. Corona R, Shah SM, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed October 8, 2023.

[3] Bellmunt J. Treatment of metastatic urothelial cancer of the bladder and urinary tract. Shah SP, ed. UptoDate. Walthman, MA: UptoDate Inc. www.uptodate.com. Accessed October 8, 2023.

[4] SEER Cancer Stat Facts: Bladder Cancer. National Cancer Institute. Bethesda, MD. Available online at seer.cancer.gov. Accessed October 8, 2023.

[5] American Cancer Society. Key Statistics for Bladder Cancer. Available online at www.cancer.org/cancer/bladder-cancer/about/key-statistics.html. Accessed October 8, 2023.

[6] Atkins MB, Bakouny Z, Choueiri TK. Epidemiology, pathology, and pathogenesis of renal cell carcinoma. Shah SP, ed. UptoDate. Walthman, MA: UptoDate Inc. www.uptodate.com. Accessed October 8, 2023.

[7] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 8, 2023.

[8] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Merkel Cell Carcinoma (v.1.2023 – April 10, 2023). Accessed October 8, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

[9] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer (v.3.2023 – May 25, 2023). Accessed October 8, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

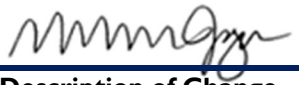
[10] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Kidney Cancer (v.1.2024 – June 21, 2023). Accessed October 8, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

[11] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. PMID 7165009.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

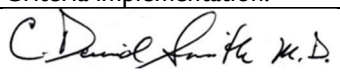
Criteria Change History

Change Date	Changed By	Description of Change	Version
	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
10/20/2023	CAC	Annual review. Removed "Accelerated Approval" information from Overview table regarding MCC indication (full FDA approval received effective 9/6/2023). Updated statistics in Descriptive Overview. Updated NCCN Guidelines. Added dosing into the criteria.	5
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/21/2022	CAC	Annual review. Updated annual cancer statistics where applicable, as well as NCCN guideline references (no changes to actual guidelines noted).	4
Signature William (Bill) Jagiello, DO			

Criteria Change History *(continued)*

Change Date	Changed By	Description of Change	Version
10/15/2021	CAC	Annual review.	3
Signature			
William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
10/18/2019	CAC	Added "or renal cell carcinoma" to criteria 1.	2
Signature			
William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
10/19/2017	Medical Director	Criteria implementation.	1
Signature			
C. David Smith			

CAC = Medicaid Clinical Advisory Committee