



Medication Policy Manual

Policy No: dru499

Topic: Bavencio®, avelumab

Date of Origin: July 14, 2017

Committee Approval Date: July 14, 2017

Next Review Date: July 2018

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Avelumab (Bavencio) is an intravenously administered immunotherapy used in the management of Merkel cell carcinoma and urothelial carcinoma (bladder cancer). It belongs to a class of medications called programmed death-ligand (PD-L1) blocking antibodies.

Policy/Criteria

I. Most contracts require prior authorization approval of avelumab (Bavencio) prior to coverage. Avelumab (Bavencio) may be considered medically necessary when criteria A, B, and C below are met.

A. One of the following (criteria 1 or 2) below is met:

1. A diagnosis of **metastatic Merkel cell carcinoma**.

OR

2. A diagnosis of **locally advanced or metastatic urothelial carcinoma (bladder cancer)** when criteria i or ii below are met:

i. There has been progression of disease during or following platinum-containing chemotherapy.

OR

ii. There has been progression of disease within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

AND

B. Avelumab (Bavencio) will be used as monotherapy.

AND

C. The patient has received no prior therapy with programmed death receptor-1 (PD-1) blocking antibody (PD-1 inhibitor) or programmed death-ligand 1 (PD-L1) blocking antibody therapy (see *Appendix 1*).

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx does not consider avelumab (Bavencio) to be a self-administered medication.

B. When prior authorization is approved, avelumab (Bavencio) may be authorized in quantities of up to 10 mg/kg every 2weeks.

C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Avelumab (Bavencio) is considered investigational when used for all other conditions, including but not limited to:

A. Gastric or gastroesophageal junction (GEJ) adenocarcinoma

B. Non-small cell lung cancer (NSCLC)

Position Statement

Summary

- Avelumab (Bavencio) is a programmed death-ligand 1 (PD-L1) blocking antibody (immunotherapy) used as a single-agent therapy in the treatment of Merkel cell carcinoma and urothelial carcinoma. ^[1]
- It is unknown if avelumab (Bavencio) provides a benefit in these two populations with regard to improvement in any clinically meaningful outcome. For both indications, avelumab (Bavencio) was approved via the FDA's Accelerated approval pathway based on tumor response [also known as objective response rate (ORR)] and duration of response.
 - * ORR has not been shown to correlate with any clinically relevant outcome (e.g. survival, symptom control, or quality of life) in either of these conditions.
 - * In clinical studies, there was no comparator employed, so the safety and effectiveness of avelumab (Bavencio) relative to other therapies or to best supportive care is not known.
- **Merkel cell carcinoma:**
 - * Avelumab (Bavencio) is approved for the treatment of metastatic Merkel cell carcinoma, regardless of prior therapy.
 - * The study for which avelumab (Bavencio) received FDA-approval in Merkel cell carcinoma only included patients who had received at least one prior line of systemic chemotherapy in the metastatic setting. Use in treatment naïve patients was extrapolated from this study. There is an ongoing study in the front-line setting. ^[2,3]
 - * Chemotherapy historically has been the standard approach for advanced Merkel cell carcinoma. Although Merkel cell carcinoma appears to be chemosensitive, the duration of response is limited. The impact of chemotherapy on survival in patients with metastatic Merkel cell carcinoma is unclear. ^[4]
- **Urothelial carcinoma:**
 - * Avelumab (Bavencio) is approved for the treatment of locally advanced or metastatic urothelial carcinoma who have had disease progression during or following platinum-containing chemotherapy or who have had disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. ^[1]
 - * Platinum-based chemotherapy is the standard of care for the first-line treatment of advanced urothelial carcinoma as it is associated with improved survival.
 - * There is no standard therapy once disease progresses after first-line treatment; however, single-agent chemotherapy has been used in this setting.
 - * Avelumab (Bavencio) has not been studied as a first-line therapy for urothelial carcinoma, including in patients unable to tolerate platinum-containing chemotherapy.

- National Comprehensive Cancer Network (NCCN) guidelines have not yet been updated since the approval of avelumab (Bavencio) in Merkel cell carcinoma. The currently preferred treatment option is enrollment in a clinical trial. [4] For bladder cancer, NCCN includes avelumab (Bavencio) as one of many options for subsequent systemic therapy for locally advanced or metastatic bladder cancer. [5]
- Avelumab (Bavencio) may cause immune-mediated pneumonitis, hepatitis, colitis, endocrinopathies, and nephritis.
- It is intravenously administered every two weeks and dosing is weight-based (10 mg/kg).
- Avelumab (Bavencio) is being investigated in other conditions including gastric cancer and NSCLC. Current evidence in these conditions is preliminary.

Clinical Efficacy

MERKEL CELL CARCINOMA

- FDA approval for avelumab (Bavencio) was based on results from a single-group, open-label (observational) trial that evaluated avelumab (Bavencio) in patients with stage IV (metastatic) Merkel cell carcinoma that had progressed after cytotoxic chemotherapy. [3]
 - * The study reported ORR as its primary endpoint. The clinical meaningfulness of this endpoint is unclear, as it has not been correlated with any clinically relevant outcome.
 - * An overall ORR of 33% was reported in the trial. The duration of response ranged from 2.8 months to upwards of 23 months.
- The relative safety and effectiveness of avelumab (Bavencio) are unknown as it has not been compared with either best supportive care, or with any other therapy.

UROTHELIAL CANCER (BLADDER CANCER)

- FDA approval for avelumab (Bavencio) was based on results from one unpublished, phase 1, non-blinded, single-arm cohort from a larger study evaluating tumor response in a variety of solid tumors. [1,6]
 - * The trial evaluated ORR as the primary endpoint. ORR is not a validated surrogate endpoint. It has not been shown to accurately predict any clinically relevant benefit in locally advanced or metastatic bladder cancer.
 - * The ORR was 14.8% and the duration of response was not estimable.
- Avelumab (Bavencio) has not been compared to any other treatment for bladder cancer.
- Avelumab (Bavencio) has not been studied as a first-line therapy for bladder cancer.

Investigational Uses

- Avelumab (Bavencio) is actively being studied to determine if there is benefit in treating other types of cancers including gastric or gastroesophageal junction adenocarcinoma and NSCLC. [7] To date, there are no studies establishing a clinical benefit in these settings.

- There is an early phase, published study evaluating avelumab (Bavencio) in NSCLC. [8] However, larger, well-controlled studies are necessary to establish the safety and effectiveness of avelumab (Bavencio) in this setting.

OmedaRx performs independent analyses of oncology medications. The OmedaRx analysis and coverage policy may differ from NCCN clinical practice guidelines.

Appendix 1: FDA-approved PD-1 and PD-L1 blocking monoclonal antibody therapies
<i>Programmed death receptor-1 (PD-1) inhibitors</i>
nivolumab, Opdivo®
pembrolizumab, Keytruda®,
<i>Programmed death-ligand 1 (PD-L1) inhibitor</i>
atezolizumab (Tecentriq™)
avelumab (Bavencio®)
durvalumab (Imfinzi™)

Cross References
Imfinzi™, durvalumab, Medication Policy Manual, Policy No. dru500
Keytruda®, pembrolizumab, Medication Policy Manual, Policy No.
Opdivo®, nivolumab, Medication Policy Manual, Policy No. dru390
Tecentriq®, atezolizumab, Medication Policy Manual, Policy No. dru463

Codes	Number	Description
HCPCS	J3590	Unclassified biologics
HCPCS	J3490	Unclassified drugs
HCPCS	J9999	Not otherwise classified, antineoplastic drugs

References

1. Bavencio® (avelumab) [package insert]. Rockland, MA: EMD Serono, Inc.; May 2017.
2. Center for Drug Evaluation and Research; U.S. Food and Drug Administration Multi-Discipline Review BLA 761049; Bavencio (avelumab). [cited 05/05/2017]; Available from:
https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/761049Orig1s000MultidisciplineR.pdf.
3. Kaufman, HL, Russell, J, Hamid, O, et al. Avelumab in patients with chemotherapy-refractory metastatic Merkel cell carcinoma: a multicentre, single-group, open-label, phase 2 trial. *The Lancet Oncology*. 2016 Oct;17(10):1374-85. PMID: 27592805
4. NCCN Clinical Practice Guidelines in Oncology™. Merkel Cell Carcinoma v.1.2017. [cited 4/5/17]; Available from:
https://www.nccn.org/professionals/physician_gls/pdf/mcc.pdf
5. NCCN Clinical Practice Guidelines in Oncology™. Bladder cancer v.4.2017. [cited 5/19/2017]; Available from:
https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf
6. Product Dossier: Bavencio® (avelumab). Rockland, MA; May 2017. EMD Serono, Inc. Date reviewed: May 31, 2017.
7. Clinicaltrials.gov. [cited (updated periodically)]; Available from: <http://clinicaltrials.gov/>
8. Gulley, JL, Rajan, A, Spigel, DR, et al. Avelumab for patients with previously treated metastatic or recurrent non-small-cell lung cancer (JAVELIN Solid Tumor): dose-expansion cohort of a multicentre, open-label, phase 1b trial. *The Lancet Oncology*. 2017 May;18(5):599-610. PMID: 28373005

Revision History

Revision Date	Revision Summary
07/14/2017	New policy