Medical Drug Clinical Criteria

Subject:	Bavencio (avelumab) injection		
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Overview

This document addresses the use of Bavencio (avelumab). Bavencio is a programmed death ligand-1 (PD-L1) antibody primarily used to treat metastatic Merkel cell carcinoma and locally advanced or metastatic urothelial carcinoma.

The FDA approved indications for Bavencio include metastatic Merkel cell carcinoma and locally advanced or metastatic urothelial carcinoma. Merkel cell carcinoma is a rare, aggressive type of skin cancer. It is considered to be aggressive because it can grow quickly and spread and it returns after treatment. Primary treatment for Merkel cell carcinoma is surgery. Urothelial carcinoma is the most common type of bladder cancer and occurs in the urinary tract system, involving the bladder and related organs. The FDA also approved for use in advanced renal cell carcinoma as first-line therapy in combination with axitinib (Inlyta). NCCN Compendia also provides a 2A recommendation for use as a single agent in Merkel cell carcinoma, for use in combination with axitinib in renal cell carcinoma for first-line therapy.

NCCN Compendia and guidelines recommend the use of Bavencio as a 2A recommendation in endometrial cancer as a single agent as second-line treatment in recurrent or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors. There are no references, but approval was based on extrapolation from the studies of prior FDA approved indications.

NCCN Compendia and guidelines recommend the use of Bavencio in metastatic (stage IV) bladder cancer, specifically primary carcinoma of the urethra as a first-line maintenance regimen (NCCN 1) if there is no progression on first-line platinum containing chemotherapy (Powles 2020). NCCN Compendia also recommends as a NCCN 2A recommendation for the use of Bavencio in metastatic bladder cancer as monotherapy, in second-line therapy for those who are post-platinum therapy or who received a therapy other than platinum or a checkpoint inhibitor in first-line therapy (Apolo 2017).

The National Comprehensive Cancer Network (NCCN) gives a category 2A recommendation for Bavencio as useful in certain circumstances as single-agent therapy for multiagent chemotherapy-resistant gestational trophoblastic neoplasia. At this time, there is only one trial (You B, et al 2020) providing data.

Definitions and Measures

Disease Progression: Cancer that continues to grow or spread.

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 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, for example, 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

Immune checkpoint inhibitor: A type of drug that blocks certain proteins made by some types of immune system cells, such as T cells, and some cancer cells. When these proteins are blocked, the "brakes" on the immune system are released and T cells are able to kill cancer cells better. Examples of checkpoint proteins found on T cells or cancer cells include programmed death (PD)-1, PD-ligand 1 (PD-L1), and cytotoxic T-lymphocyte–associated antigen (CTLA)-4/B7-1/B7-2.

Merkel cell carcinoma: A rare, aggressive skin cancer.

Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.

Monoclonal antibody: A protein developed in the laboratory that can locate and bind to specific substances in the body and on the surface of cancer cells.

Programmed death (PD)-1 proteins: PD-1 proteins are found on T-cells and attach to PD ligands (PD-L1) found on normal (and cancer) cells (see immune checkpoint inhibitor above). Normally, this process keeps T-cells from attacking other cells in the body. However, this can also prevent T-cells from attacking cancer cells in the body. Examples of FDA approved anti-PD-1 agents include Keytruda (pembrolizumab), Opdivo (nivolumab), and Libtayo (cemiplimab).

Programmed death ligand (PD-L)-1: The ligands found on normal (and cancer) cells to which the PD-1 proteins attach (see immune checkpoint inhibitor above). Cancer cells can have large amounts of PD-L1 on their surface, which helps them to avoid immune attacks. Examples of FDA approved anti-PD-L1 agents include Bavencio (avelumab), Tecentriq (atezolizumab), and Imfinzi (durvalumab).

Urothelial carcinoma: A type of bladder cancer which occurs in the urinary tract system.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Bavencio (avelumab)

Requests for Bavencio (avelumab) may be approved if the following criteria are met:

I. Individual is 12 years of age or older; **AND**
   - A. Individual has a diagnosis of metastatic Merkel cell carcinoma (Label NCCN 2A); **AND**
   - B. Individual has a current ECOG performance status of 0-2**; AND**
   - C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   - D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

II. Individual has a diagnosis of locally advanced or metastatic Urothelial Carcinoma (Label, NCCN 1); **AND**
   - A. Individual is using agent as monotherapy; **AND**
   - B. Individual has a current ECOG performance status of 0-2; **AND**
   - C. Individual meets *one* of the following:
     1. Individual is using after platinum-containing chemotherapy (either as subsequent therapy after disease progression during or following platinum regimen, ***or*** as maintenance therapy following completion of platinum regimen with no evidence of disease progression); **OR**
     2. Has confirmed disease progression within 12 months of receiving neoadjuvant or adjuvant treatment with platinum-containing chemotherapy;

   AND
   - D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   - E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

III. Individual has a diagnosis of multi-agent chemotherapy-resistant gestational trophoblastic neoplasia (NCCN 2A); **AND**
   - A. Individual has intermediate OR high-risk disease; **AND**
   - B. Individual is using as single-agent therapy; **AND**
   - C. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   - D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

~~III.~~IV. Individual has a diagnosis of endometrial carcinoma (NCCN 2A); **AND**
   - A. Individual is using for recurrent or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors; **AND**
   - B. Individual is using as monotherapy; **AND**
   - C. Individual is using as second-line treatment or subsequent therapy; **AND**
   - D. Individual has a current ECOG performance status of 0-2; **AND**
   - E. Individual has not received treatment with another anti-PD1 or anti-PD-L1 agent; **AND**
   - F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

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OR

~~IV.~~V. Individual has a diagnosis of advanced Renal Cell Carcinoma (RCC) (Label, NCCN 2A); **AND**

A. Individual is using as first-line therapy; **AND**
B. Individual is using in combination with axitinib (Inlyta); **AND**
C. Individual has histological confirmation of RCC with clear cell component; **AND**
D. Individual has a current ECOG performance status of 0-2; **AND**
E. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

Requests for Bavencio (avelumab) may not be approved when the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9023	Injection, avelumab, 10 mg [Bavencio]

ICD-10 Diagnosis

C4A.0-C4A.9	Merkel cell carcinoma
C54.1	Malignant neoplasm of endometrium
C58	Malignant neoplasm of placenta
C61	Malignant neoplasm of prostate
C64.1-C64.9	Malignant neoplasm of kidney
C65.1-C65.9	Malignant neoplasm of renal pelvis
C66.1-C66.9	Malignant neoplasm of ureter
C67.0-C67.9	Malignant neoplasm of bladder
C68.0	Malignant neoplasm of urethra
C7B.1	Secondary Merkel cell carcinoma
Z85.51	Personal history of malignant neoplasm of bladder
Z85.59	Personal history of malignant neoplasm of other urinary tract organ

Document History

Revised: 02/23/2024
Document History:

- 02/23/2024 – Annual Review: Add NCCN 2A criteria for use in gestational trophoblastic neoplasia. Coding Reviewed: Added ICD-10-CM C58.
- 02/24/2023 – Annual Review: Add clarifying criteria to NCCN 2A recommendation for use as subsequent therapy in endometrial cancer. Minor wording and formatting updates. Coding Reviewed: Added ICD-10-CM C54.1.
- 02/25/2022 – Annual Review: Add NCCN 2A recommendation for use in endometrial cancer. Update references for Bladder cancer with NCCN. Coding Reviewed: No changes.
- 02/19/2021 – Annual Review: Update criteria to clarify use in urothelial carcinoma for subsequent therapy. Coding Reviewed: No changes.
- 08/21/2020 – Select Review: Update criteria to allow maintenance use in urothelial carcinoma after platinum-containing regimen per FDA label. Coding review: Added ICD-10-CM Z85.59
- 02/21/2020 – Annual Review: Minor wording and formatting changes. Coding Review: No changes
- 08/16/2019 – Select Review: Update Bavencio criteria to restrict use in those with prior anti-PD-1/PD-L1 agent therapy for consistency. Coding reviewed: No changes.
- 05/17/2019 – Annual Review: Initial review of Bavencio (avelumab). Add new clinical criteria for new FDA indication in advanced renal cell carcinoma as first-line therapy in combination with axitinib (Inlyta). Minor wording and formatting changes. Coding reviewed: Added ICD-10 C64.1-C64.9 Renal Cell Carcinoma.

References

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2024. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 9, 2024
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on December 30, 2023.
    a. Bladder Cancer. V3.2023. Revised May 25, 2023.
    b. Gestational Trophoblastic Neoplasia. V1.2024. Revised October 24, 2023.
    c. Kidney Cancer. V2.2024. Revised January 3, 2024.
    d. Merkel Cell Carcinoma: V1.2024. Revised November 22, 2023.
    e. Uterine Neoplasms. V1.2024. Revised September 20, 2023.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.