

<b>POLICY NUMBER</b> UM_1306	<b>SUBJECT</b> Bavencio™ (avelumab)	<b>DEPT/PROGRAM</b> UM Dept	<b>PAGE 1 OF 4</b>
<b>DATE REVIEWED</b> 04/05/17, 04/06/18, 04/05/19	<b>APPROVAL DATE</b> April 10, 2019	<b>EFFECTIVE DATE</b> April 10, 2019	<b>REVISION DATES</b> (latest version listed last) 04/12/17, 04/11/18, 04/10/19
<b>PRIMARY BUSINESS OWNER:</b> <b>APPROVED BY:</b> Dr. Andrew Hertler		<b>COMMITTEE/BOARD APPROVAL</b> Utilization Management Committee	
<b>URAC STANDARDS</b> HUM 1		<b>ADDITIONAL AREAS OF IMPACT</b>	
<b>CMS REQUIREMENTS</b>	<b>STATE/FEDERAL REQUIREMENTS</b>	<b>APPLICABLE LINES OF BUSINESS</b> Oncology	

**I. PURPOSE**

To define and describe the accepted indications for Bavencio (avelumab) usage in the treatment of cancer.

**II. DEFINITIONS**

**Bavencio (avelumab):** is a human IgG1 lambda monoclonal antibody that binds to the programmed death ligand-1 (PD-L1) found on T-cells and blocks the interaction of PD-L1 with PD-1 and B7.1 receptors on the tumor cell. Blocking the PD-1/PD-L1 pathway improves the anti-tumor immune response by reducing immunosuppressive signals between immune cells and tumor cells. Additionally, avelumab induced antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.

Bavencio (avelumab) is FDA approved for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC). It is also FDA approved for patients with locally advanced or metastatic urothelial carcinoma (UC) who have disease progression during, following, or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Bavencio (avelumab) is available in 200 mg single dose vials.

**III. POLICY**

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

**Inclusion Criteria:** Bavencio (avelumab) may be considered medically necessary when any of the following selection criteria is met:

**1. Merkel Cell Carcinoma (MCC)**

- a. The member has stage IV MCC **AND**
- b. Bavencio (avelumab) is being used as a single agent.

**2. Urothelial Carcinoma (UC)**

- a. The member has clinical stage IIIB, IVA, IVB, recurrent, or metastatic UC

- b. Bavencio (avelumab) is being used as a single agent for subsequent systemic therapy post-platinum.

**Exclusion Criteria:** Bavencio (avelumab) is not considered medically necessary when any of the following selection criteria is met:

1. Bavencio (avelumab) is being used after disease progression with the same regimen or prior PD-L1 inhibitor.
2. Concurrent use with other anticancer treatments, steroids, or immunosuppressive agents.
3. Dosing exceeds single dose limit of Bavencio (avelumab) 10mg/kg.
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

#### IV. PROCEDURE

Requests for Bavencio (avelumab) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:** 800 mg over 60 minutes every 2 weeks until disease progression. All patients should receive premedication with an antihistamine (e.g., diphenhydramine) and acetaminophen 30 to 60 minutes prior to the first 4 avelumab infusions; premedication may be administered prior to subsequent doses as necessary.
2. **Dosage Adjustments:**
  - a. Renal dysfunction and nephritis, serum creatinine more than 1.5 and up to 6 times ULN: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and withhold avelumab until resolution to Grade 0 or 1 toxicity. May resume after resolution and corticosteroid taper.
  - b. Renal dysfunction and nephritis, serum creatinine more than 6 times ULN: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and permanently discontinue avelumab.
  - c. Hepatitis, AST or ALT more than 3 and up to 5 times ULN or total bilirubin more than 1.5 and up to 3 times ULN: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and withhold avelumab until resolution to Grade 0 or 1 toxicity. May resume after resolution and corticosteroid taper.
  - d. Hepatitis, AST or ALT more than 5 times ULN or total bilirubin more than 3 times ULN: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and permanently discontinue avelumab.
  - e. Colitis, Grade 2 or 3: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and withhold avelumab until resolution to Grade 0 or 1 toxicity. May resume after resolution and corticosteroid taper.
  - f. Colitis, Grade 4 or recurrent Grade 3: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and permanently discontinue avelumab.
  - g. Diarrhea, Grade 2 or 3: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and withhold avelumab until resolution to Grade 0 or 1 toxicity. May resume after resolution and corticosteroid taper.

- h. Diarrhea, Grade 4 or recurrent Grade 3: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and permanently discontinue avelumab.
- i. Endocrinopathies (e.g., hypothyroidism, hyperthyroidism, adrenal insufficiency, hyperglycemia), Grade 3 or 4: Withhold avelumab and initiate appropriate medical management of toxicity. May resume after resolution Grade 0 or 1 and corticosteroid taper.
- j. Immune-mediated toxicity, persistent Grade 2 or 3 (lasting 12 weeks or longer): Permanently discontinue use.
- k. Infusion-related reaction, Grade 1 or 2: Interrupt or slow infusion rate.
- l. Infusion-related reaction, Grade 3 or 4: Permanently discontinue use.
- m. Pneumonitis, Grade 2: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and withhold avelumab until resolution to Grade 0 or 1 toxicity. May resume after resolution and corticosteroid taper.
- n. Pneumonitis, Grade 3 or 4 or recurrent Grade 2: Administer corticosteroids 1 to 2 mg/kg/day prednisone or equivalents followed by taper and permanently discontinue avelumab.
- o. Other immune-mediated toxicity, moderate or severe: Withhold avelumab during medical evaluation and initiate high dose corticosteroids and if appropriate, hormone replacement therapy. Upon improvement to Grade 1 or less, initiate corticosteroid taper. May resume avelumab if toxicity remains at Grade 1 or less after completion of corticosteroid taper.
- p. Other immune-mediated toxicity, life-threatening (excluding endocrinopathies) or recurrent severe: Permanently discontinue use.
- q. Requirement for 10 mg/day or greater prednisone or equivalent for more than 12 weeks: Permanently discontinue use.

### 3. Monitoring

- a. Evidence of disease response or stabilization may indicate efficacy.
- b. Hyperglycemia or other signs or symptoms of diabetes.
- c. Liver function tests: Prior to initiation and periodically during therapy.
- d. Serum creatinine: Prior to initiation and periodically during treatment.
- e. Thyroid function changes: At initiation and periodically during treatment, and as clinically indicated.
- f. Signs and symptoms of adrenal insufficiency.
- g. Signs and symptoms of colitis.
- h. Signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria.
- i. Signs and symptoms of pneumonitis: If suspected evaluate with radiographic imaging.

## V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

## VI. ATTACHMENTS

None

## VII. REFERENCES

1. Bavencio PI prescribing information. EMD Serono, Inc. Rockland, MA 2018.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.