

BAVENCIO® (avelumab) is the **FIRST** and **ONLY** immunotherapy indicated for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy.¹



Electronic Health Record (EHR) Instructions

Creating a Patient List With Appropriate Patients for BAVENCIO® (avelumab) in the Epic® EHR System



Actor Portrayals



Avelumab is the only National Comprehensive Cancer Network® (NCCN®) **Category 1** and **Preferred** immunotherapy option for maintenance therapy for both cisplatin-eligible and cisplatin-ineligible patients with locally advanced or metastatic UC that has not progressed on first-line platinum-containing chemotherapy²

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Preferred intervention: Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.

SELECT IMPORTANT SAFETY INFORMATION

BAVENCIO can cause **severe and fatal immune-mediated adverse reactions** in any organ system or tissue and at any time after starting treatment with a PD-1/PD-L1 blocking antibody, including after discontinuation of treatment.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Please see Important Safety Information [here](#) and full Prescribing Information [here](#).



Instructions for Creating a Patient List

BAVENCIO is indicated for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy.¹

These instructions are designed to help identify appropriate BAVENCIO patients. These instructions are specifically used to create a patient list in the Epic system and will not work for other conditions, treatments, or therapeutic areas or on other EHR systems.

The suggested criteria and process outlined in these instructions are variable, and not all steps will apply to every medical group. Any steps or settings that are not part of a medical group’s standard process should be excluded or modified accordingly. Any questions should be directed to the appropriate service provider. The availability of the suggested criteria may vary and depends on documentation practices. The medical group is solely responsible for implementing, testing, monitoring, and ongoing operation of any EHR tools.

Suggested Criteria

Diagnosis: International Classification of Diseases, Tenth Revision (ICD-10) codes³

C67	Malignant neoplasm of bladder
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
C65	Malignant neoplasm of the renal pelvis
C65.1	Malignant neoplasm of the right renal pelvis
C65.2	Malignant neoplasm of the left renal pelvis
C65.9	Malignant neoplasm of the unspecified renal pelvis
C66	Malignant neoplasm of the ureter
C66.1	Malignant neoplasm of the right ureter
C66.2	Malignant neoplasm of the left ureter
C66.9	Malignant neoplasm of the unspecified ureter
C68.0	Malignant neoplasm of urethra
Z85.51	Personal history of malignant neoplasm of bladder

Medications¹

Prior use of platinum-based chemotherapy:

- Cisplatin
- Carboplatin

Locally advanced or metastatic disease (staging TNM)^{4,5}

1. Tumor status: T4b
Nodal status: N1-3
Metastatic status: M1

or

2. Overall cancer stage: 3/4

Note: Depending on how information was documented in the EHR, staging information may not always be available in structured data. Consider running the patient query and confirm the patient’s staging information with a manual chart evaluation.

The ICD-10-CM diagnosis codes listed above are provided only as examples of potentially relevant codes.

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Epic Instructions

Consider using Epic's reporting functionality to identify patients by leveraging Reporting Workbench to create the patient list. Consult your organization if administrative user rights are required to access this functionality.

Optional: A diagnosis grouper for UC and medication grouper for platinum-based therapies may be available. The use of groupers is optional but may be considered when the user is familiar with the grouper concept. Creating new groupers requires administrative rights and is optional for the queries below.

1. Access Reporting Workbench (click the Epic logo > Reports > My Reports)
2. Navigate to the Library tab from the Reports menu
3. Enter "generic criteria" or "find patients" in the search field and click Search
4. Select the Find My Patients – Generic Criteria report and click + New report
5. In the Report Settings window, select the Criteria tab and add the first criterion to the query
6. In the Find Criteria field, enter "diagnosis" and select the Diagnosis by Code criterion (note: when using groupers, select Diagnosis by Grouper and select the ovarian cancer diagnosis grouper)
7. Enter and select all suggested ICD-10 codes for urothelial cancer (C67, C65, C66, C68.0, Z85.51)
Note: when using the diagnosis grouper criterion, consider the EDG Concept and ICD urothelial grouper records
8. In the Find Criteria field, enter "medication" and select the Meds: All time, by simple generic name criterion (alternatively, consider the Meds: All time, by exact medication or Meds: All time, by pharmacological class)
9. Enter and select the desired treatments (cisplatin, carboplatin)
Note: when using the medication grouper criterion, consider the ERX platinum-based chemotherapy grouper records
10. Set the logic to include patients with any of the urothelial cancer ICD-10 codes, and include patients with one or more of the platinum-based treatments
11. Select the Display tab to set all display columns for the report. Search for any display information in the Available Columns pane. Select all desired columns and click the right arrow to drag to the Selected Columns pane
12. In the General tab, enter the desired Report Name and Description (for example, "Platinum-responsive OR treated locally advanced or metastatic urothelial cancer patients")
13. Click Save and Run to create the patient list. The list will display all patients matching the criteria. Use the filters to narrow down the patient list or export to Excel

Note: the Oncology Generic Criteria report template may be used too. Consider the Plan: Diagnosis or Plan: Diagnosis by grouper criteria for the diagnoses, and the Order Medication or Procedures by grouper or Patient: Medication history by medication criterion for medications. Staging information may be available in the Patient: SmartData element value criterion.



Notes

The medical groups shall be solely responsible for implementation, testing, and monitoring of the instructions to ensure proper orientation in each medical group's EHR system.

Capabilities, functionality, and setup (customization) for each individual EHR system vary. EMD Serono is not responsible for revising the implementation instructions it provides to any medical group.

While EMD Serono tests its implementation instructions, the instructions are not guaranteed to work for all available EHR systems, and EMD Serono shall have no liability therefor.

While EHRs may assist providers in identifying appropriate patients for consideration of assessment and treatment, the decision and action should ultimately be decided by a healthcare provider in consultation with the patient, after a review of the patient's records to determine eligibility.

The instructions have not been designed to and are not tools and/or solutions for meeting Advancing Care Information and/or any other quality/accreditation requirement.

Reference to these EHRs is not intended to imply affiliation with or sponsorship of the EHR manufacturer and/or its affiliates.



INDICATIONS

BAVENCIO® (avelumab) is indicated for:

- The maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy
- The treatment of patients with locally advanced or metastatic UC who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

IMPORTANT SAFETY INFORMATION

BAVENCIO can cause **severe and fatal immune-mediated adverse reactions** in any organ system or tissue and at any time after starting treatment with a PD-1/PD-L1 blocking antibody, including after discontinuation of treatment.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

No dose reduction for BAVENCIO is recommended. For immune-mediated adverse reactions, withhold or permanently discontinue BAVENCIO depending on severity. In general, withhold BAVENCIO for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue BAVENCIO for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids. In general, if BAVENCIO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy. Toxicity management guidelines for adverse reactions that do not necessarily require systemic corticosteroids (eg, endocrinopathies and dermatologic reactions) are discussed in subsequent sections.

BAVENCIO can cause **immune-mediated pneumonitis**. Withhold BAVENCIO for Grade 2, and permanently discontinue for Grade 3 or Grade 4 pneumonitis. Immune-mediated pneumonitis occurred in 1.1% (21/1854) of patients, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (0.3%), and Grade 2 (0.6%) adverse reactions. Systemic corticosteroids were required in all (21/21) patients with pneumonitis.

BAVENCIO can cause **immune-mediated colitis**. The primary component of immune-mediated colitis consisted of diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Withhold BAVENCIO for Grade 2 or Grade 3, and permanently discontinue for Grade 4 colitis. Immune-mediated colitis occurred in 1.5% (27/1854) of patients, including Grade 3 (0.4%) and Grade 2 (0.8%) adverse reactions. Systemic corticosteroids were required in all (27/27) patients with colitis.

BAVENCIO can cause **hepatotoxicity and immune-mediated hepatitis**. Withhold or permanently discontinue BAVENCIO based on tumor involvement of the liver and severity of aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total bilirubin elevation. Immune-mediated hepatitis occurred with BAVENCIO as a single agent in 1.1% (20/1854) of patients, including fatal (0.1%), Grade 3 (0.8%), and Grade 2 (0.2%) adverse reactions. Systemic corticosteroids were required in all (20/20) patients with hepatitis.

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IMPORTANT SAFETY INFORMATION (continued)

BAVENCIO can cause primary or secondary **immune-mediated adrenal insufficiency**. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement, as clinically indicated. Withhold BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated adrenal insufficiency occurred in 0.6% (11/1854) of patients, including Grade 3 (0.1%) and Grade 2 (0.4%) adverse reactions. Systemic corticosteroids were required in all (11/11) patients with adrenal insufficiency.

BAVENCIO can cause **immune-mediated hypophysitis**. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement, as clinically indicated. Withhold BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated pituitary disorders occurred in 0.1% (1/1854) of patients, which was a Grade 2 (0.1%) adverse reaction.

BAVENCIO can cause **immune-mediated thyroid disorders**. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism, as clinically indicated. Withhold BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Thyroiditis occurred in 0.2% (4/1854) of patients, including Grade 2 (0.1%) adverse reactions. Hyperthyroidism occurred in 0.4% (8/1854) of patients, including Grade 2 (0.3%) adverse reactions. Systemic corticosteroids were required in 25% (2/8) of patients with hyperthyroidism. Hypothyroidism occurred in 5% (97/1854) of patients, including Grade 3 (0.2%) and Grade 2 (3.6%) adverse reactions. Systemic corticosteroids were required in 6% (6/97) of patients with hypothyroidism.

BAVENCIO can cause **immune-mediated type I diabetes mellitus**, which can present with diabetic ketoacidosis. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated type I diabetes mellitus occurred in 0.2% (3/1854) of patients, including Grade 3 (0.2%) adverse reactions.

BAVENCIO can cause **immune-mediated nephritis with renal dysfunction**. Withhold BAVENCIO for Grade 2 or Grade 3, and permanently discontinue for Grade 4 increased blood creatinine. Immune-mediated nephritis with renal dysfunction occurred in 0.1% (2/1854) of patients, including Grade 3 (0.1%) and Grade 2 (0.1%) adverse reactions. Systemic corticosteroids were required in all (2/2) patients with nephritis with renal dysfunction.

BAVENCIO can cause **immune-mediated dermatologic adverse reactions**, including rash or dermatitis. Exfoliative dermatitis including Stevens Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold BAVENCIO for suspected and permanently discontinue for confirmed SJS, TEN, or DRESS. Immune-mediated dermatologic adverse reactions occurred in 6% (108/1854) of patients, including Grade 3 (0.1%) and Grade 2 (1.9%) adverse reactions. Systemic corticosteroids were required in 25% (27/108) of patients with dermatologic adverse reactions.

BAVENCIO can result in **other immune-mediated adverse reactions**. Other clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in patients who received BAVENCIO or were reported with the use of other PD-1/PD-L1 blocking antibodies. For **myocarditis**, permanently discontinue BAVENCIO for Grade 2, Grade 3, or Grade 4. For **neurological toxicities**, withhold BAVENCIO for Grade 2 and permanently discontinue for Grade 3 or Grade 4.

BAVENCIO can cause severe or life-threatening **infusion-related reactions**. Premedicate patients with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent infusions based upon clinical

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IMPORTANT SAFETY INFORMATION (continued)

judgment and presence/severity of prior infusion reactions. Monitor patients for signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 infusion-related reactions. Permanently discontinue BAVENCIO for Grade 3 or Grade 4 infusion-related reactions. Infusion-related reactions occurred in 26% of patients, including three (0.2%) Grade 4 and ten (0.5%) Grade 3 infusion-related reactions. Eleven (85%) of the 13 patients with Grade ≥ 3 reactions were treated with intravenous corticosteroids.

Fatal and other serious **complications of allogeneic hematopoietic stem cell transplantation (HSCT)** can occur in patients who receive HSCT before or after being treated with a PD-1/PD-L1 blocking antibody. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

BAVENCIO can cause **fetal harm** when administered to a pregnant woman. Advise patients of the potential risk to a fetus including the risk of fetal death. Advise females of childbearing potential to use effective contraception during treatment with BAVENCIO and for at least 1 month after the last dose of BAVENCIO. It is not known whether BAVENCIO is excreted in human milk. Advise a lactating woman **not to breastfeed** during treatment and for at least 1 month after the last dose of BAVENCIO due to the potential for serious adverse reactions in breastfed infants.

A **fatal adverse reaction** (sepsis) occurred in one (0.3%) patient with **locally advanced or metastatic urothelial carcinoma (UC)** receiving BAVENCIO + best supportive care (BSC) as first-line maintenance treatment. In patients with previously treated locally advanced or metastatic UC, fourteen patients (6%) who were treated with BAVENCIO experienced either pneumonitis, respiratory failure, sepsis/urosepsis, cerebrovascular accident, or gastrointestinal adverse events, which led to death.

The most common adverse reactions (all grades, $\geq 20\%$) in patients with **locally advanced or metastatic UC** receiving BAVENCIO + BSC (vs BSC alone) as first-line maintenance treatment were fatigue (35% vs 13%), musculoskeletal pain (24% vs 15%), urinary tract infection (20% vs 11%), and rash (20% vs 2.3%). In patients with previously treated locally advanced or metastatic UC receiving BAVENCIO, the most common adverse reactions (all grades, $\geq 20\%$) were fatigue, infusion-related reaction, musculoskeletal pain, nausea, decreased appetite, and urinary tract infection.

Selected laboratory abnormalities worsening from baseline (all grades, $\geq 20\%$) in patients with **locally advanced or metastatic UC** receiving BAVENCIO + BSC (vs BSC alone) as first-line maintenance treatment were blood triglycerides increased (34% vs 28%), alkaline phosphatase increased (30% vs 20%), blood sodium decreased (28% vs 20%), lipase increased (25% vs 16%), aspartate aminotransferase (AST) increased (24% vs 12%), blood potassium increased (24% vs 16%), alanine aminotransferase (ALT) increased (24% vs 12%), blood cholesterol increased (22% vs 16%), serum amylase increased (21% vs 12%), hemoglobin decreased (28% vs 18%), and white blood cell decreased (20% vs 10%).

Please see full Prescribing Information [here](#).

References: **1.** Bavencio [prescribing information]. Rockland, MA: EMD Serono, Inc. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Bladder Cancer V.3.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed August 16, 2023. To view the most recent and complete version of the guideline, 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. **3.** National Center for Health Statistics. – ICD-10-CM. Centers for Disease Control and Prevention website. <https://icd10cmtool.cdc.gov/?fy=FY2023>. Accessed July 26, 2023. **4.** Data on file. EMD Serono, Inc. **5.** Brierly JD, Gospodarowicz MK, Wittekind C, ed. *TNM Classification of Malignant Tumors*. 8th ed. Hoboken, NJ: Wiley Blackwell; 2017.



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