BAVENCIO® avelumab Injection 20 mg/mL

BAVENCIO
Nurse Handbook

The ONLY immunotherapy approved in the first-line maintenance setting

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.

NCCN CATEGORY 1 & PREFERRED

National Comprehensive Cancer Network® (NCCN®) Recommendation

Avelumab maintenance is the only NCCN **CATEGORY 1** and **PREFERRED** immunotherapy option for both cisplatin-eligible and -ineligible patients with locally advanced or metastatic UC that has not progressed on first-line platinum-containing chemotherapy.[1]

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.

SELECTED 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.

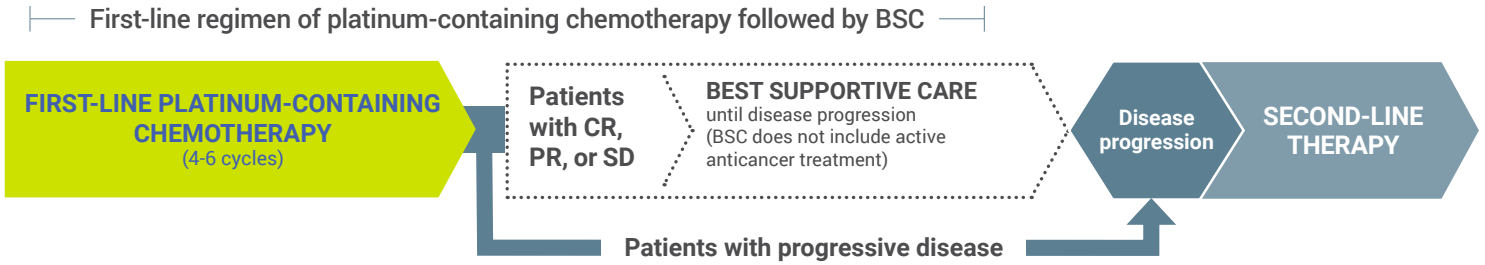
Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, 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 Selected Safety Information throughout and full Prescribing Information here.

Table of contents

This handbook is intended to provide you with important information as you care for patients who have been prescribed BAVENCIO® (avelumab) as maintenance treatment after their locally advanced or metastatic UC did not progress with first-line platinum-containing chemotherapy. This handbook can be used as your go-to for BAVENCIO-related information. It discusses JAVELIN Bladder 100 Trial data, Warnings and Precautions, adverse reactions, dosing and administration, and dose modifications. A discussion guide has also been included at the end of this handbook to help facilitate conversations with your patients about their treatment questions and needs.

Platinum-containing chemotherapy* followed by best supportive care (BSC)† is effective, but many patients progress within 9 months[2-4]



- **~60%** to **90%** of patients with unresectable, locally advanced or metastatic UC are eligible to receive first-line platinum-containing chemotherapy[5-8]
- **~50%** to **70%** of patients are cisplatin chemotherapy eligible[9]

- **~50%** to **75%** of patients achieve disease control (CR, PR, or SD) with first-line platinum-containing chemotherapy, but most progress within **9 months**[2-4]

- **~27%** to **35%** of patients receive second-line treatment[5-7,10]

~9 to **15 months** is the median overall survival range for patients treated with first-line platinum-containing chemotherapy followed by BSC[4‡]

*Platinum-containing therapy in first-line treatment includes gemcitabine + cisplatin, gemcitabine + carboplatin, and a dose-dense combination of methotrexate, vinblastine, doxorubicin, and cisplatin with growth factor support.[1]

†BSC excludes systemic antitumor therapy.[4]

‡14-15 months mOS for patients treated with cisplatin-containing regimens and 9-10 months mOS for patients treated with carboplatin-containing regimens.[4]

CR=complete response; mOS=median overall survival; PR=partial response; SD=stable disease.

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What is BAVENCIO® (avelumab) maintenance therapy?

BAVENCIO is the ONLY immunotherapy approved for the first-line maintenance treatment of patients with locally advanced or metastatic UC that has not progressed following treatment with platinum-containing chemotherapy

BAVENCIO maintenance therapy is not second-line treatment. It is part of a first-line treatment regimen that can help patients live longer

First-line maintenance treatment with BAVENCIO + best supportive care (BSC)* was investigated to determine whether it could prolong overall survival vs BSC alone in patients who did not progress on first-line platinum-containing chemotherapy[4†]

- In the JAVELIN Bladder 100 Trial, 72% of patients achieved either a complete response or partial response and 28% of patients achieved stable disease prior to randomization

*BSC excludes systemic antitumor therapy.[4]

†Platinum-containing therapy in first-line treatment includes gemcitabine + cisplatin, gemcitabine + carboplatin, and a dose-dense combination of methotrexate, vinblastine, doxorubicin, and cisplatin with growth factor support.[1]

CR=complete response; PR=partial response; SD=stable disease.

SELECTED SAFETY INFORMATION

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.

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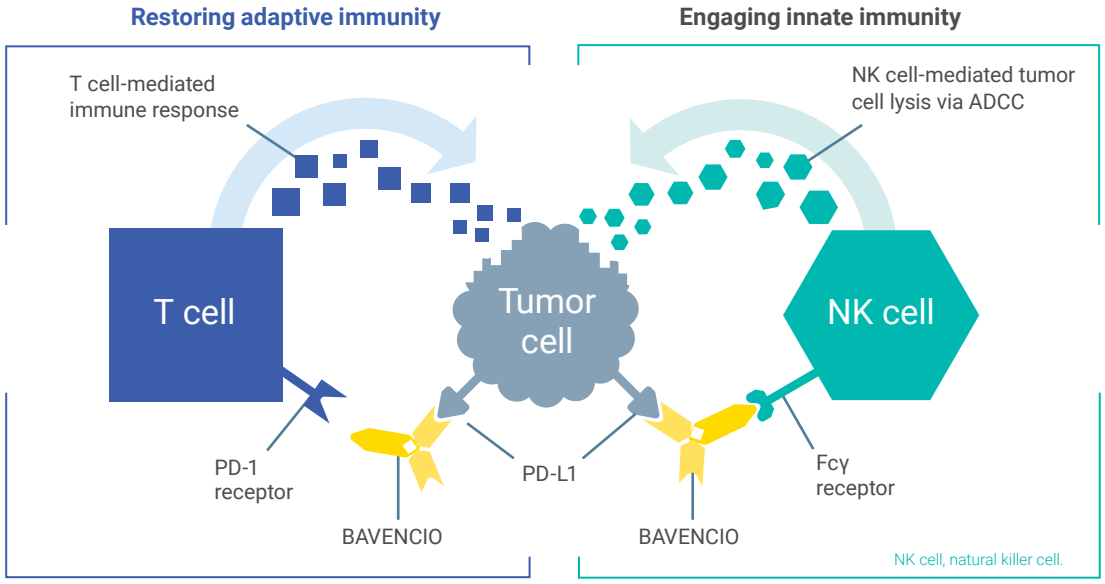
Mechanism of action

BAVENCIO® (avelumab) engages both the adaptive and innate immune systems[11]



Preclinical and in vitro data may not necessarily correlate with clinical outcomes.

ADAPTIVE IMMUNE RESPONSE

BAVENCIO has been shown to release the suppression of the T cell-mediated antitumor immune response by blocking the interaction of PD-L1 with PD-1 receptors in preclinical models

INNATE IMMUNE RESPONSE

BAVENCIO has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro

SELECTED SAFETY INFORMATION

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 1.2% (21/1738) 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% (26/1738) of patients, including Grade 3 (0.4%) and Grade 2 (0.7%) adverse reactions. Systemic corticosteroids were required in all (26/26) patients with colitis.

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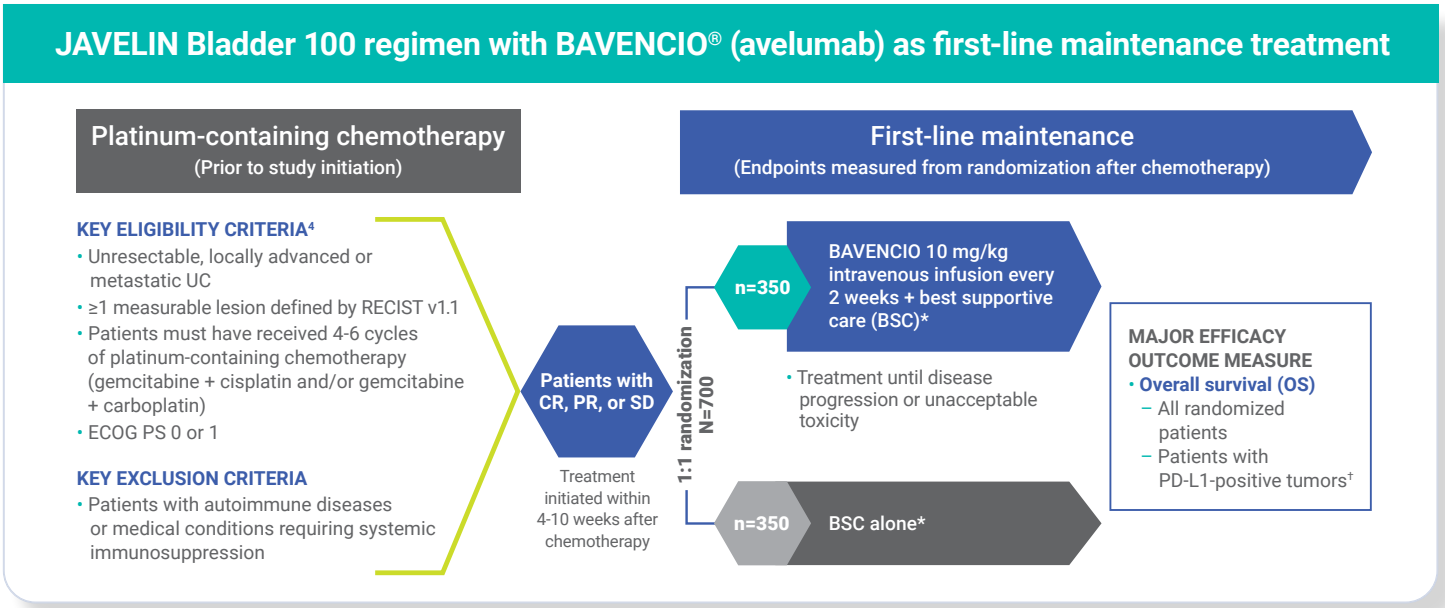
Study design

JAVELIN Bladder 100 Trial—a Phase 3, randomized, open-label, multicenter study in patients with unresectable, locally advanced or metastatic urothelial carcinoma that did not progress with first-line platinum-containing chemotherapy (N=700)[4]



- Stratified by best response to chemotherapy (CR/PR [72%] vs SD [28%] per RECIST v1.1) and site of metastasis (visceral [55%] vs nonvisceral, including bone metastasis [45%]) assessed at the time of initiating first-line platinum-containing chemotherapy[4]
- First-line chemotherapy regimens included prior gemcitabine plus cisplatin (56%), prior gemcitabine plus carboplatin (38%), and prior gemcitabine plus cisplatin and gemcitabine plus carboplatin (6%)
- Administration of BAVENCIO was permitted beyond RECIST-defined disease progression if the patient was clinically stable and considered to be deriving clinical benefit by the investigator
- Assessment of tumor status was performed at baseline, 8 weeks after randomization, then every 8 weeks up to 12 months after randomization, and every 12 weeks thereafter until documented confirmed disease progression based on BICR assessment per RECIST v1.1

*BSC was administered as deemed appropriate by the treating physician, and could include treatment with antibiotics, nutritional support, and other patient management approaches with palliative intent (excludes systemic antitumor therapy).[4]

†PD-L1 expression was assessed in tumor samples using the VENTANA PD-L1 (SP263) assay.[4]

BICR=blinded independent central review; CR=complete response; ECOG PS=Eastern Cooperative Oncology Group (ECOG) Performance Status; PD-L1=programmed cell death ligand-1; PR=partial response; RECIST=Response Evaluation Criteria in Solid Tumors; SD=stable disease.

SELECTED SAFETY INFORMATION

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 0.9% (16/1738) of patients, including fatal (0.1%), Grade 3 (0.6%), and Grade 2 (0.1%) adverse reactions. Systemic corticosteroids were required in all (16/16) patients with hepatitis.

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 0.5% (8/1738) of patients, including Grade 3 (0.1%) and Grade 2 (0.3%) adverse reactions. Systemic corticosteroids were required in all (8/8) patients with adrenal insufficiency.

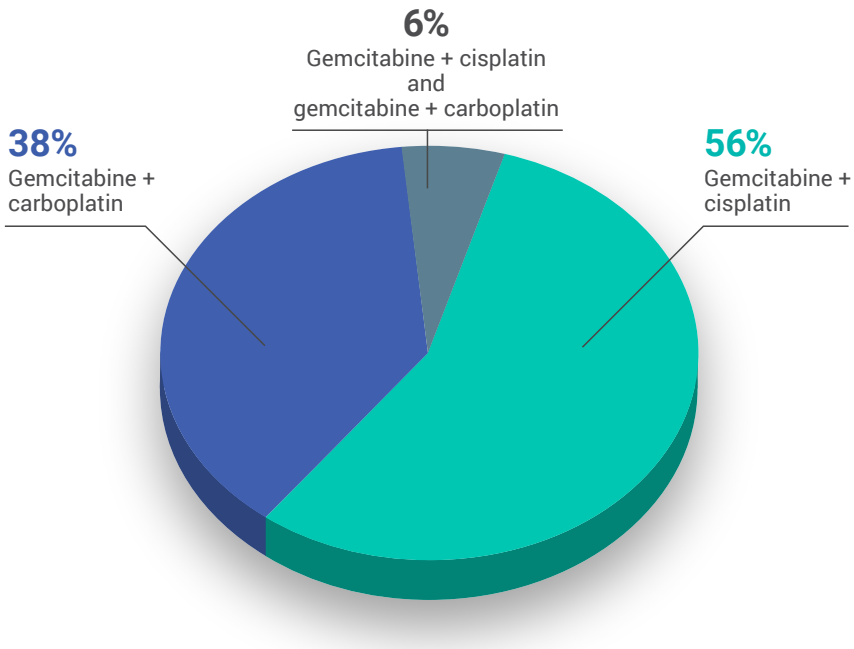
Patient characteristics

Selected baseline characteristics of all randomized patients in the study (N=700)

Median age, years (range)	69 (32, 90)
≥65 years	66%
≥75 years	24%
Male	77%
Race	
White	67%
Asian	22%
ECOG PS	
0	61%
1	39%

PD-L1 tumor status*	
PD-L1-positive	51%
PD-L1-negative	39%
Unknown	10%
Sites of metastasis prior to chemotherapy (stratification factor)	
Visceral	55%
Nonvisceral	45%
Best response to first-line chemotherapy (stratification factor)	
CR or PR	72%
SD	28%

First-line chemotherapy regimen



*Using the VENTANA PD-L1 (SP263) assay, PD-L1-positive status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively. If none of these criteria were met, PD-L1 status was considered negative.[4]

CR=complete response; ECOG PS=Eastern Cooperative Oncology Group (ECOG) Performance Status; PD-L1=programmed cell death ligand-1; PR=partial response; SD=stable disease.

SELECTED SAFETY INFORMATION

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% (1/1738) 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% (4/1738) of patients, including Grade 2 (0.1%) adverse reactions. Hyperthyroidism occurred in 0.4% (7/1738) of patients, including Grade 2 (0.3%) adverse reactions. Systemic corticosteroids were required in 29% (2/7) of patients with hyperthyroidism. Hypothyroidism occurred in 5% (90/1738) of patients, including Grade 3 (0.2%) and Grade 2 (3.7%) adverse reactions. Systemic corticosteroids were required in 7% (6/90) of patients with hypothyroidism.

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Clinical data

JAVELIN Bladder 100 Trial—a Phase 3, randomized, open-label, multicenter study in patients with unresectable, locally advanced or metastatic urothelial carcinoma that did not progress with first-line platinum-containing chemotherapy (N=700)[4]

BAVENCIO® (avelumab) + best supportive care (BSC) demonstrated superior overall survival (OS) vs BSC alone[4]

Primary OS analysis:
OS in all randomized patients, data cutoff October 21, 2019[4]

Hazard ratio (HR): 0.69
(95% CI: 0.56, 0.86); 2-sided *P*-value=0.001
P-value based on stratified log-rank

21.4 months median OS		**14.3 months median OS**
BAVENCIO® (avelumab) + BSC	**vs**	**BSC alone**
(95% CI: 18.9, 26.1); n=350		(95% CI: 12.9, 17.9); n=350

31% reduction in risk of death vs BSC alone

7.1 months improvement in median OS

- A pre-planned interim analysis (IA) occurred with a data cutoff of October 21, 2019. The IA was considered the primary analysis of the trial, since the primary endpoint was met[12]
- Median duration of follow-up was 19.6 months (95% CI: 18.0, 20.6) in the BAVENCIO + BSC arm and 19.2 months (95% CI: 17.4, 21.6) in the BSC arm[12]

OS in patients with PD-L1-positive tumors* (major efficacy outcome measure)

- BAVENCIO + BSC demonstrated statistically significant improvement in OS vs BSC alone in patients with PD-L1-positive tumors (n=358, 51%); the OS hazard ratio was 0.56 (95% CI: 0.40, 0.79; 2-sided *P*-value <0.001)[4]

OS in patients with PD-L1-negative tumors* (exploratory analysis)

- In patients with PD-L1-negative tumors (n=270, 39%), the OS hazard ratio was 0.85 (95% CI: 0.62, 1.18)[4]

*Using the VENTANA PD-L1 (SP263) assay, PD-L1-positive status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively. If none of these criteria were met, PD-L1 status was considered negative.[5]

CI=confidence interval; PD-L1=programmed death-ligand 1.

SELECTED SAFETY INFORMATION

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 0.1% (2/1738) of patients, including Grade 3 (0.1%) 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% (1/1738) of patients, which was a Grade 2 (0.1%) adverse reaction. Systemic corticosteroids were required in this patient.

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LIMITATIONS: Although the follow-up overall survival (OS) analysis was prespecified, no formal hypothesis testing was performed given that the OS endpoint was met in the initial interim analysis. Therefore, no conclusions can be drawn from the follow-up OS analysis.[12]

Follow-up OS analysis: BAVENCIO + best supportive care (BSC) vs BSC alone[12]

OS in all randomized patients (N=700), data cutoff June 4, 2021[12]

Hazard ratio (HR): 0.76
(95% CI: 0.63, 0.92)

23.8 months median OS	VS	**15.0 months median OS**
BAVENCIO + BSC (n=350)		**BSC (n=350)**
(95% CI: 19.9, 28.8)		(95% CI: 13.5, 18.2)

- Median duration of follow-up was 38.0 months (95% CI: 36.1, 40.5) in the BAVENCIO + BSC arm and 39.6 months (95% CI: 36.2, 41.7) in the BSC arm alone[12]

Follow-up OS results in patients with PD-L1-positive tumors*

- In patients with PD-L1-positive tumors (n=358, 51%), the OS hazard ratio was 0.69 (95% CI: 0.52, 0.90)

Follow-up OS results in patients with PD-L1-negative tumors* (exploratory analysis)

- In patients with PD-L1-negative tumors (n=270, 39%), the OS hazard ratio was 0.82 (95% CI: 0.62, 1.09)

*Using the VENTANA PD-L1 (SP263) assay, PD-L1- positive status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively. If none of these criteria were met, PD-L1 status was considered negative.[4]
CI=confidence interval; PD-1=programmed death ligand-1.

SELECTED SAFETY INFORMATION

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 5% (90/1738) of patients, including Grade 3 (0.1%) and Grade 2 (2.0%) adverse reactions. Systemic corticosteroids were required in 29% (26/90) 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.

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BAVENCIO® (avelumab)—safety profile

The WARNINGS AND PRECAUTIONS were established based on data from over 1700 patients treated with BAVENCIO 10 mg/kg across multiple tumor types, the majority of whom were treated with BAVENCIO monotherapy.

Summary of warnings and precautions

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
  - Upon improvement to Grade ≤1, initiate corticosteroid taper and continue to taper over ≥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 1.2% (21/1738) 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% (26/1738) of patients, including Grade 3 (0.4%) and Grade 2 (0.7%) adverse reactions
- Systemic corticosteroids were required in all (26/26) patients with colitis

(Summary of warnings and precautions continues on next page)

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Summary of warnings and precautions (cont'd)

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 0.9% (16/1738) of patients, including fatal (0.1%), Grade 3 (0.6%), and Grade 2 (0.1%) adverse reactions
- Systemic corticosteroids were required in all (16/16) patients with hepatitis

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 0.5% (8/1738) of patients, including Grade 3 (0.1%) and Grade 2 (0.3%) adverse reactions
- Systemic corticosteroids were required in all (8/8) 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% (1/1738) 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% (4/1738) of patients, including Grade 2 (0.1%) adverse reactions
- Hyperthyroidism occurred in 0.4% (7/1738) of patients, including Grade 2 (0.3%) adverse reactions
  - Systemic corticosteroids were required in 29% (2/7) of patients with hyperthyroidism
- Hypothyroidism occurred in 5% (90/1738) of patients, including Grade 3 (0.2%) and Grade 2 (3.7%) adverse reactions
  - Systemic corticosteroids were required in 7% (6/90) of patients with hypothyroidism

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Summary of warnings and precautions (cont'd)

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 0.1% (2/1738) of patients, including Grade 3 (0.1%) 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% (1/1738) of patients, which was a Grade 2 (0.1%) adverse reaction. Systemic corticosteroids were required in this patient

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 5% (90/1738) of patients, including Grade 3 (0.1%) and Grade 2 (2.0%) adverse reactions
- Systemic corticosteroids were required in 29% (26/90) 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 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 25% of patients, including three (0.2%) Grade 4 and nine (0.5%) Grade 3 infusion-related reactions
- Eleven (92%) of the 12 patients with Grade ≥3 reactions were treated with intravenous corticosteroids

(Summary of warnings and precautions continues on next page)

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Summary of warnings and precautions (cont'd)

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

Primary analysis, data cutoff October 21, 2019[4]

JAVELIN Bladder 100 Trial—a Phase 3, randomized, open-label, multicenter study in patients with unresectable, locally advanced or metastatic urothelial carcinoma that did not progress with first-line platinum-containing chemotherapy (N=689)[4]

Selected adverse reactions

Fatal adverse reaction	A fatal adverse reaction (sepsis) occurred in **one (0.3%) patient** receiving BAVENCIO + best supportive care (BSC)
Serious adverse reactions	Serious adverse reactions occurred in **28% of patients** receiving BAVENCIO + BSC. Serious adverse reactions in ≥1% of patients included urinary tract infection (including kidney infection, pyelonephritis, and urosepsis) (6.1%), pain (including abdominal, back, bone, flank, extremity, and pelvic pain) (3.2%), acute kidney injury (1.7%), hematuria (1.5%), sepsis (1.2%), and infusion-related reaction (1.2%)
Infusion-related reactions	Patients received premedication with an antihistamine and acetaminophen prior to each infusion. Infusion-related reactions occurred in **10% of patients** treated with BAVENCIO + BSC (Grade 3: 0.9%)
Oral steroid use	**Thirty-one (9%) patients** treated with BAVENCIO + BSC received an oral prednisone dose equivalent to ≥40 mg daily for an immune-mediated adverse reaction

BAVENCIO® (avelumab)—safety profile

Primary analysis, data cutoff October 21, 2019[4]

JAVELIN Bladder 100 Trial—a Phase 3, randomized, open-label, multicenter study in patients with unresectable, locally advanced or metastatic urothelial carcinoma that did not progress with first-line platinum-containing chemotherapy (N=689)[4]

Adverse reactions (≥10%) of patients receiving BAVENCIO + best supportive care (BSC)

Adverse Reactions	BAVENCIO + BSC (n=344)		BSC (n=345)	
	All Grades %	Grades 3-4 %	All Grades %	Grades 3-4 %
General Disorders and Administration Site Conditions				
Fatigue*	35	1.7	13	1.7
Pyrexia	15	0.3	3.5	0
Musculoskeletal and Connective Tissue Disorders				
Musculoskeletal pain†	24	1.2	15	2.6
Arthralgia	16	0.6	6	0
Skin and Subcutaneous Tissue Disorders				
Rash‡	20	1.2	2.3	0
Pruritus	17	0.3	1.7	0
Infections and Infestations				
Urinary tract infection§	20	6	11	3.8
Gastrointestinal Disorders				
Diarrhea	17	0.6	4.9	0.3
Constipation	16	0.6	9	0
Nausea	16	0.3	6	0.6
Vomiting	13	1.2	3.5	0.6
Respiratory, Thoracic and Mediastinal Disorders				
Cough‖	14	0.3	4.6	0
Metabolism and Nutrition Disorders				
Decreased appetite	14	0.3	7	0.6
Endocrine Disorders				
Hypothyroidism	12	0.3	0.6	0
Injury, Poisoning and Procedural Complications				
Infusion-related reaction	10	0.9	0	0

*Fatigue is a composite term that includes fatigue, asthenia, and malaise.

†Musculoskeletal pain is a composite term that includes musculoskeletal pain, back pain, myalgia, and neck pain.

‡Rash is a composite term that includes rash, rash maculo-papular, erythema, dermatitis acneiform, eczema, erythema multiforme, rash erythematous, rash macular, rash papular, rash pruritic, drug eruption, and lichen planus.

§Urinary tract infection is a composite term that includes urinary tract infection, urosepsis, cystitis, kidney infection, pyuria, pyelonephritis, bacteriuria, pyelonephritis acute, urinary tract infection bacterial, and Escherichia urinary tract infection.

‖Cough is a composite term that includes cough and productive cough.

Please see Selected Safety Information throughout and full Prescribing Information here.

BAVENCIO® avelumab Injection 20 mg/mL

BAVENCIO® (avelumab)—safety profile

Primary analysis, data cutoff October 21, 2019[4]

JAVELIN Bladder 100 Trial—a Phase 3, randomized, open-label, multicenter study in patients with unresectable, locally advanced or metastatic urothelial carcinoma that did not progress with first-line platinum-containing chemotherapy (N=689)[4]

Discontinuation rates due to an adverse reaction

- In the BAVENCIO + best supportive care (BSC) arm (n=344), permanent discontinuation due to an adverse reaction occurred in **12%** of patients
  - Adverse reactions resulting in permanent discontinuation of BAVENCIO in >1% of patients were myocardial infarction (including acute myocardial infarction and troponin T increased) **(1.5%)** and infusion-related reaction **(1.2%)**

Dose interruptions due to an adverse reaction

- In the BAVENCIO + BSC arm (n=344), dose interruptions due to an adverse reaction, excluding temporary interruptions of BAVENCIO infusions due to infusion-related reactions, occurred in **41%** of patients
  - Adverse reactions leading to interruption of BAVENCIO in >2% of patients were urinary tract infection (including pyelonephritis) **(4.7%)** and blood creatinine increased (including acute kidney injury, renal impairment, and renal failure) **(3.8%)**

Selected laboratory abnormalities worsening from baseline occurring in ≥10% of patients receiving BAVENCIO + BSC

Laboratory Abnormality	BAVENCIO + BSC*		BSC*	
	Any Grade %	Grades 3-4 %	Any Grade %	Grades 3-4 %
Chemistry				
Blood triglycerides increased	34	2.1	28	1.2
Alkaline phosphatase increased	30	2.9	20	2.3
Blood sodium decreased	28	6	20	2.6
Lipase increased	25	8	16	6
Aspartate aminotransferase (AST) increased	24	1.7	12	0.9
Blood potassium increased	24	3.8	16	0.9
Alanine aminotransferase (ALT) increased	24	2.6	12	0.6
Blood cholesterol increased	22	1.2	16	0.3
Serum amylase increased	21	5	12	1.8
CPK increased	19	2.4	12	0
Phosphate decreased	19	3.2	15	1.2
Hematology				
Hemoglobin decreased	28	4.4	18	3.2
White blood cell decreased	20	0.6	10	0
Platelet count decreased	18	0.6	12	0.3

*Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: BAVENCIO + BSC group (range: 339 to 344 patients) and BSC group (range: 329 to 341 patients).

Please see Selected Safety Information throughout and full Prescribing Information here.

BAVENCIO® avelumab Injection 20 mg/mL

BAVENCIO® (avelumab) dosing

Recommended dosage

800 mg IV infusion over 60 minutes every 2 weeks

- **BAVENCIO is administered as an intravenous infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity**
- BAVENCIO is supplied in 200 mg/10 mL vials; therefore, 4 vials are used for the recommended 800 mg dose

Premedication

- Premedicate patients with an antihistamine and with acetaminophen prior to the first 4 infusions of BAVENCIO
- Premedication should be administered for subsequent BAVENCIO doses based on clinical judgment and presence/severity of prior infusion reactions

SELECTED SAFETY INFORMATION

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 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 25% of patients, including three (0.2%) Grade 4 and nine (0.5%) Grade 3 infusion-related reactions. Eleven (92%) of the 12 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.

Please see Selected Safety Information throughout and full Prescribing Information here.

BAVENCIO® avelumab Injection 20 mg/mL

Preparation, storage, and administration

Preparation

- **Visually inspect vial** for particulate matter and discoloration. BAVENCIO® (avelumab) is a clear, colorless to slightly yellow solution. Discard vial if the solution is cloudy, discolored, or contains particulate matter
- **Withdraw the required volume of BAVENCIO** from the vial(s) and inject it into a 250 mL infusion bag containing either 0.9% Sodium Chloride Injection or 0.45% Sodium Chloride Injection
- **Gently invert the bag to mix the diluted solution**, avoid foaming or excessive shearing
- **Inspect the solution** to ensure it is clear, colorless, and free of visible particles
- **Discard any partially used or empty vials**

Injection: 200 mg/10 mL (20 mg/mL) solution for infusion in a single-dose vial.

Storage of diluted solution

Protect from light.

- **Store diluted BAVENCIO solution**
  - At room temperature up to 77° F (25° C) for no more than 4 hours from the time of dilution, **or**
  - Under refrigeration at 36° F to 46° F (2° C to 8° C) for no more than 24 hours from the time of dilution. If refrigerated, allow the diluted solution to come to room temperature prior to administration

Do not freeze or shake the diluted solution.

Administration

- **Administer the diluted solution over 60 minutes** through an intravenous line containing a sterile, nonpyrogenic, low protein binding in-line filter (pore size of 0.2 micron)
- **Do not coadminister other drugs** through the same intravenous line

SELECTED SAFETY INFORMATION

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.

Important information on selected adverse reactions with BAVENCIO® (avelumab)

- The data below and on the following pages related to immune-mediated adverse reactions and infusion-related reactions are based on data from over 1700 patients treated with BAVENCIO 10 mg/kg across multiple tumor types, the majority of whom were treated with BAVENCIO monotherapy

Severe and fatal immune-mediated adverse reactions

- BAVENCIO is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death-receptor 1 (PD-1) or the PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions
- Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions
- **Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue and at any time after starting treatment with a PD-1/PD-L1 blocking antibody**
  - While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, they can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies

Monitor and Assess

- 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

General Dose Modifications

- No dose reduction for BAVENCIO is recommended
- 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
  - Dosage modifications for BAVENCIO for adverse reactions that require management different from these general guidelines are summarized on the following pages

General Corticosteroid Management

- 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 on the following pages

Advise your patients that the adverse reactions listed in this guide are not all the possible side effects of treatment. Ask your patients to contact their cancer care team right away if they notice any signs or symptoms of adverse reactions. They may report side effects to FDA at 1-800-FDA-1088.

Immune-mediated pneumonitis

Clinical trial experience (across the development program)

- BAVENCIO® (avelumab) can cause immune-mediated pneumonitis
- Across clinical studies,* immune-mediated pneumonitis occurred in 1.2% (21/1738) of patients receiving BAVENCIO, including:
  - Fatal (0.1%) adverse reactions
  - Grade 4 (0.1%) adverse reactions
  - Grade 3 (0.3%) adverse reactions
  - Grade 2 (0.6%) adverse reactions
- Pneumonitis led to permanent discontinuation of BAVENCIO in 0.3% and withholding of BAVENCIO in 0.3% of patients
- Systemic corticosteroids were required in all (21/21) patients with pneumonitis
- Pneumonitis resolved in 57% (12/21) of the patients
- Of the 5 patients in whom BAVENCIO was withheld for pneumonitis, 5 reinitiated treatment with BAVENCIO after symptom improvement
  - Of these, none had recurrence of pneumonitis
- With other PD-1/PD-L1 blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation

Median time to onset 2.5 months Range: 3 days to 11 months[6]

Median duration 1.75 months Range: 4 days to 4+ months[6]

MONITOR

Monitor patients for signs and symptoms of pneumonitis, including

Cough	Shortness of breath	Chest pain

ASSESS

Assess the severity of the adverse reaction[7]

Grade 1	Grade 2	Grade 3	Grade 4
Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; medical intervention indicated; limiting instrumental ADL	Severe symptoms; limiting self-care ADL; oxygen indicated	Life-threatening respiratory compromise; urgent intervention indicated (eg, tracheotomy or intubation)

MODIFY

Modify treatment based on severity

Withhold†	Permanently discontinue
For Grade 2	For Grade 3 or 4

- 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

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.

†Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of last dose or inability to reduce prednisone to 10 mg per day or less (or equivalent) within 12 weeks of initiating corticosteroids.

ADL=activities of daily living.

Immune-mediated colitis

Clinical trial experience (across the development program)

- BAVENCIO® (avelumab) can cause immune-mediated colitis
- Across clinical studies,* immune-mediated colitis occurred in 1.5% (26/1738) of patients receiving BAVENCIO, including:
  - Grade 3 (0.4%) adverse reactions
  - Grade 2 (0.7%) adverse reactions
- Colitis led to permanent discontinuation of BAVENCIO in 0.5% and withholding of BAVENCIO in 0.5% of patients
- Systemic corticosteroids were required in all (26/26) patients with colitis
- Colitis resolved in 69% (18/26) of the patients
- Of the 8 patients in whom BAVENCIO was withheld for colitis, 5 reinitiated treatment with BAVENCIO after symptom improvement
  - Of these, 40% had recurrence of colitis

Median time to onset 2.1 months Range: 2 days to 11 months[6]

Median duration 1.5 months Range: 1 day to 14+ months[6]

MONITOR

Monitor patients for signs and symptoms of colitis, including

Diarrhea	Stools that are black, tarry, sticky, or have blood or mucus	Severe abdominal pain

- The primary component of the immune-mediated colitis consisted of diarrhea
- Cytomegalovirus (CMV) 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

ASSESS

Assess the severity of the adverse reaction[7]

Grade 1	Grade 2	Grade 3	Grade 4
Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Abdominal pain; mucus or blood in stool	Severe abdominal pain; peritoneal signs	Life-threatening consequences; urgent intervention indicated

MODIFY

Modify treatment based on severity

Withhold†	Permanently discontinue
For Grade 2 or 3	For Grade 4

- 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

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.

†Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of last dose or inability to reduce prednisone to 10 mg per day or less (or equivalent) within 12 weeks of initiating corticosteroids.

Hepatotoxicity and immune-mediated hepatitis

Clinical trial experience (across the development program)

- BAVENCIO® (avelumab) can cause immune-mediated hepatitis
- Across clinical studies,* immune-mediated hepatitis occurred in 0.9% (16/1738) of patients receiving BAVENCIO, including:
  - Fatal (0.1%) adverse reactions
  - Grade 3 (0.6%) adverse reactions
  - Grade 2 (0.1%) adverse reactions
- Hepatitis led to permanent discontinuation of BAVENCIO in 0.5% and withholding of BAVENCIO in 0.2% of patients
- Systemic corticosteroids were required in all (16/16) patients with hepatitis
- Hepatitis resolved in 56% (9/16) of the patients
- Of the 3 patients in whom BAVENCIO was withheld for hepatitis, 3 reinitiated treatment with BAVENCIO after symptom improvement
  - Of these, none had recurrence of hepatitis

Median time to onset 3.2 months Range: 1 week to 15 months[6]

Median duration 2.5 months Range: 1 day to 7.4+ months[6]

MONITOR

Monitor patients for signs and symptoms of hepatitis, including

Jaundice	Severe nausea or vomiting	Pain on the right side of abdomen
Dark urine	Easy bruising or bleeding	

- Evaluate liver enzymes at baseline and periodically during treatment

ASSESS

Assess the severity of the adverse reaction[7]

Grade 1	Grade 2	Grade 3	Grade 4
Asymptomatic, intervention not indicated	Moderate symptoms; medical intervention indicated	Symptomatic liver dysfunction; fibrosis by biopsy; compensated cirrhosis; hospitalization or prolongation of existing hospitalization indicated	Life-threatening consequences; severe decompensated liver function (eg, coagulopathy, encephalopathy, coma)

MODIFY

Modify treatment based on severity

	Withhold†	Permanently discontinue
Hepatitis with no tumor involvement of the liver	For AST or ALT increases >3 and up to 8 times ULN, or total bilirubin increases >1.5 and up to 3 times ULN	For AST or ALT >8 times ULN or total bilirubin >3 times ULN
Hepatitis with tumor involvement of the liver‡	If baseline AST or ALT is >1 and up to 3 times ULN and increases to >5 and up to 10 times ULN, or baseline AST or ALT is >3 and up to 5 times ULN and increases to >8 and up to 10 times ULN	For AST or ALT increases to >10 times ULN or total bilirubin increases to >3 times ULN

- 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

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.

†Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of last dose or inability to reduce prednisone to 10 mg per day or less (or equivalent) within 12 weeks of initiating corticosteroids.

‡If AST and ALT are less than or equal to ULN at baseline, withhold or permanently discontinue BAVENCIO based on recommendations for hepatitis where there is no tumor involvement of the liver.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

Please see Selected Safety Information throughout and full Prescribing Information here.

BAVENCIO® avelumab Injection 20 mg/mL

Immune-mediated endocrinopathies: adrenal insufficiency

Clinical trial experience (across the development program)

- BAVENCIO® (avelumab) can cause primary or secondary adrenal insufficiency
- Across clinical studies,* immune-mediated adrenal insufficiency occurred in 0.5% (8/1738) of patients receiving BAVENCIO, including:
  - Grade 3 (0.1%) adverse reactions
  - Grade 2 (0.3%) adverse reactions
- Adrenal insufficiency led to permanent discontinuation of BAVENCIO in 0.1% and withholding of BAVENCIO in 0.1% of patients
- Systemic corticosteroids were required in all (8/8) patients with adrenal insufficiency
- Adrenal insufficiency did not resolve in any patient (0/8)
- Of the 2 patients in whom BAVENCIO was withheld for adrenal insufficiency, none reinitiated treatment with BAVENCIO

Median time to onset **2.5 months** **Range:** 1 day to 8 months[6]

MONITOR

Monitor patients during and after treatment for signs and symptoms of adrenal insufficiency, including

Fatigue	Weight loss or weight gain	Dizziness or fainting
Hair loss	Changes in mood or behavior	

ASSESS

Assess the severity of the adverse reaction[7]

Grade 1	Grade 2	Grade 3	Grade 4
Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Moderate symptoms; medical intervention indicated	Severe symptoms; hospitalization indicated	Life-threatening consequences; urgent intervention indicated

MODIFY

Modify treatment based on severity

Grade 2 or higher	Grade 3-4
Initiate symptomatic treatment, including hormone replacement, as clinically indicated	Withhold BAVENCIO for adrenal insufficiency until clinically stable, or permanently discontinue depending on severity

- 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

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.

Immune-mediated endocrinopathies: hypophysitis

Clinical trial experience (across the development program)

- BAVENCIO® (avelumab) can cause immune-mediated hypophysitis. Hypophysitis can cause hypopituitarism
- Across clinical studies,* immune-mediated pituitary disorders occurred in 0.1% (1/1738) of patients receiving BAVENCIO, including:
  - Grade 2 (0.1%) adverse reactions
- Hypopituitarism did not lead to withholding of BAVENCIO in this patient
- Systemic corticosteroids were not required in this patient

MONITOR

Hypophysitis can present with acute symptoms associated with mass effect, such as

Headache	Photophobia	Visual field defects

ASSESS

Assess the severity of the adverse reaction[7]

Grade 1	Grade 2	Grade 3	Grade 4
Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated

MODIFY

Modify treatment based on severity

Any grade	Grade 3-4
Initiate hormone replacement as clinically indicated	Withhold BAVENCIO until clinically stable, or permanently discontinue depending on severity

- 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

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.

ADL=activities of daily living.

Immune-mediated endocrinopathies: thyroid disorders

Clinical trial experience (across the development program)

- BAVENCIO® (avelumab) can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism
- Across clinical studies,* thyroiditis occurred in 0.2% (4/1738) of patients receiving BAVENCIO, including:
  - Grade 2 (0.1%) adverse reactions
  - Thyroiditis did not lead to permanent discontinuation or withholding of BAVENCIO in any patients
  - No patients with thyroiditis required systemic corticosteroids
  - Thyroiditis did not resolve in any patients (0/4)
- Across clinical studies,* hyperthyroidism occurred in 0.4% (7/1738) of patients receiving BAVENCIO, including:
  - Grade 2 (0.3%) adverse reactions
  - Hyperthyroidism did not lead to permanent discontinuation of BAVENCIO in any patients and led to withholding of BAVENCIO in 0.1% of patients
  - Systemic corticosteroids were required in 29% (2/7) of patients with hyperthyroidism
  - Hyperthyroidism resolved in 86% (6/7) of the patients
  - Of the 2 patients in whom BAVENCIO was withheld for hyperthyroidism, 2 reinitiated treatment with BAVENCIO after symptom improvement; of these, none had recurrence of hyperthyroidism
- Across clinical studies,* hypothyroidism occurred in 5% (90/1738) of patients receiving BAVENCIO, including:
  - Grade 3 (0.2%) adverse reactions
  - Grade 2 (3.7%) adverse reactions
  - Hypothyroidism led to permanent discontinuation of BAVENCIO in 0.1% and withholding of BAVENCIO in 0.5% of patients
  - Systemic corticosteroids were required in 7% (6/90) of patients with hypothyroidism
  - Hypothyroidism resolved in 4% (4/90) of the patients
  - Of the 8 patients in whom BAVENCIO was withheld for hypothyroidism, none reinitiated BAVENCIO

Median time to onset 2.8 months **Range:** 3.6 weeks to 19.3 months[12]

Median duration N/E **Range:** 8 days to more than 23.9 months[12]

N/E=not estimable.

MONITOR

Monitor patients for signs and symptoms of thyroid disorders, including

Tachycardia	Increased sweating	Fatigue
Weight gain or weight loss	Unusual thirst or hunger	Hair loss
Feeling cold	Constipation	Changes in mood or behavior

ASSESS

Assess the severity of the adverse reaction[13]

Grade 1	Grade 2	Grade 3	Grade 4
Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; thyroid suppression or replacement therapy indicated; limiting instrumental ADL	Severe symptoms; limiting self-care ADL; hospitalization indicated	Life-threatening consequences; urgent intervention indicated

MODIFY

Modify treatment based on severity

Any grade hypothyroidism or hyperthyroidism	Grade 3-4
Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism, as clinically indicated	Withhold BAVENCIO until clinically stable, or permanently discontinue depending on severity

- 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

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.

ADL=activities of daily living.

Please see Selected Safety Information throughout and full Prescribing Information here.

BAVENCIO® avelumab Injection 20 mg/mL

Immune-mediated endocrinopathies: type 1 diabetes mellitus, which can present with diabetic ketoacidosis

Clinical trial experience (across the development program)

- Type 1 diabetes mellitus, which can present with diabetic ketoacidosis
- Across clinical studies,* immune-mediated type 1 diabetes mellitus occurred in 0.1% (2/1738) of patients receiving BAVENCIO® (avelumab), including:
  - Grade 3 (0.1%) adverse reactions
- Type 1 diabetes mellitus led to permanent discontinuation of BAVENCIO in these 2 patients
- Type 1 diabetes mellitus did not lead to withholding of BAVENCIO in any patient
- Systemic corticosteroids were not required in any patient with type 1 diabetes mellitus
- Type 1 diabetes mellitus resolved in no patient and all patients required ongoing insulin treatment

MONITOR

Monitor patients for hyperglycemia or other signs and symptoms of diabetes

ASSESS

Assess the severity of the adverse reaction[13]

Grade 1	Grade 2	Grade 3	Grade 4
Abnormal glucose above baseline with no medical intervention	Change in daily management from baseline for a diabetic; oral antiglycemic agent initiated; workup for diabetes	Insulin therapy initiated; hospitalization indicated	Life-threatening consequences; urgent intervention indicated

MODIFY

Modify treatment based on severity

Hyperglycemia
Initiate treatment with insulin as clinically indicated. Withhold BAVENCIO until clinically stable or permanently discontinue depending on severity

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.

Immune-mediated nephritis with renal dysfunction

Clinical trial experience (across the development program)

- BAVENCIO® (avelumab) can cause immune-mediated nephritis
- Across clinical studies,* immune-mediated nephritis with renal dysfunction occurred in 0.1% (1/1738) of patients receiving BAVENCIO, including:
  - Grade 2 (0.1%) adverse reactions
- Nephritis with renal dysfunction led to permanent discontinuation of BAVENCIO in this patient
- Nephritis did not lead to withholding of BAVENCIO in any patient
- Systemic corticosteroids were required in this patient
- Nephritis with renal dysfunction did not resolve in this patient

MONITOR

Evaluate creatinine at baseline and periodically during treatment

ASSESS

Assess the severity of the adverse reaction[13]

Grade 1 creatinine increased	Grade 2 creatinine increased	Grade 3 creatinine increased	Grade 4 creatinine increased
>ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 x baseline; >3.0 - 6.0 x ULN	>6.0 x ULN

MODIFY

Modify treatment based on severity

Withhold†	Permanently discontinue
For Grade 2 or 3 increased blood creatinine	For Grade 4 increased blood creatinine

- 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

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.

†Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of last dose or inability to reduce prednisone to 10 mg per day or less (or equivalent) within 12 weeks of initiating corticosteroids.

ULN=upper limit of normal.

Immune-mediated dermatologic adverse reactions

Clinical trial experience (across the development program)

- BAVENCIO® (avelumab) can cause immune-mediated 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
- Across clinical studies,* immune-mediated dermatologic adverse reactions occurred in 5% (90/1738) of patients receiving BAVENCIO, including:
  - Grade 3 (0.1%) adverse reactions
  - Grade 2 (2.0%) adverse reactions
- Dermatologic adverse reactions led to permanent discontinuation of BAVENCIO in 0.3% of patients and withholding of BAVENCIO in 0.4% of patients
- Systemic corticosteroids were required in 29% (26/90) of patients with dermatologic adverse reactions
  - One patient required the addition of tacrolimus to high-dose corticosteroids
- Dermatologic adverse reactions resolved in 41% (37/90) of the patients
- Of the 7 patients in whom BAVENCIO was withheld for dermatologic adverse reactions, 3 reinitiated treatment with BAVENCIO after symptom improvement
  - Of these, none had recurrence of dermatologic adverse reaction

MONITOR

Monitor patients for signs and symptoms of rash or dermatitis

Rash	Itching	Skin blistering or peeling
Painful sores or ulcers in mouth or nose, throat, or genital area	Fever or flu-like symptoms	Swollen lymph nodes

ASSESS

Assess the severity of the adverse reaction[13]

Grade 1	Grade 2	Grade 3	Grade 4
–	–	SJS - skin sloughing covering <10% BSA with asociated signs (eg, erythema, purpura, epidermal detachment, and mucous membrane detachment)	SJS - skin sloughing covering 10% to 30% BSA with associated signs TEN - skin sloughing covering ≥30% BSA with associated symptoms

MODIFY

Modify treatment based on severity

Withhold†	Permanently discontinue
For suspected SJS, TEN, or DRESS	For confirmed SJS, TEN, or DRESS

- Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes
- 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

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.

†Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of last dose or inability to reduce prednisone to 10 mg per day or less (or equivalent) within 12 weeks of initiating corticosteroids.

BSA=body surface area; DRESS=drug reaction with eosinophilia and systemic symptoms; PD-1=programmed death-1 receptor; PD-L1=programmed death ligand-1; SJS=Stevens Johnson Syndrome; TEN=toxic epidermal necrolysis.

Please see Selected Safety Information throughout and full Prescribing Information here.

BAVENCIO® avelumab Injection 20 mg/mL

Other immune-mediated adverse reactions

Clinical trial experience (across the development program)

- The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received BAVENCIO® (avelumab) or were reported with the use of other PD-1/PD-L1 blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions

Other immune-mediated adverse reactions	
Cardiac/Vascular	Myocarditis, pericarditis, vasculitis
Gastrointestinal	Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis
Nervous System	Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/ myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy
Ocular	Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada like syndrome, as this may require treatment with systemic corticosteroids to reduce the risk of permanent vision loss
Musculoskeletal and Connective Tissue	Myositis/polymyositis, rhabdomyolysis (and associated sequelae including renal failure), arthritis, polymyalgia rheumatic
Endocrine	Hypoparathyroidism
Other (Hematologic/Immune)	Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection

- For myocarditis, permanently discontinue BAVENCIO for Grade 2, Grade 3, or Grade 4 adverse reactions
- For neurological toxicities, withhold BAVENCIO for Grade 2* and permanently discontinue for Grade 3 or Grade 4 adverse reactions

*Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of last dose or inability to reduce prednisone to 10 mg per day or less (or equivalent) within 12 weeks of initiating corticosteroids.

PD-1=programmed death-1 receptor; PD-L1=programmed death ligand-1.

Infusion-related reactions

Clinical trial experience (across the development program)

- BAVENCIO® (avelumab) can cause severe or life-threatening infusion-related reactions
- Across clinical studies,* infusion-related reactions occurred in 25% (439/1738; all grades) of patients, including:
  - 3 (0.2%) Grade 4 infusion-related reactions
  - 9 (0.5%) Grade 3 infusion-related reactions
- 93% (1615/1738) of patients received premedication with antihistamine and acetaminophen
- 11 (92%) of the 12 patients with Grade ≥3 reactions were treated with intravenous corticosteroids
- 14% of patients (252/1738) had infusion-related reactions that occurred after BAVENCIO infusion was completed
- 25.3% (439/1738) of patients experienced infusion-related reactions[12]
- The onset of infusion-related reactions was mostly at the initial infusions[12]:
  - 20.1% of patients experienced their first infusion-related reaction during the first infusion (n=1738 patients at risk)
  - 4.7% of patients experienced their first infusion-related reaction during their second infusion (n=1306 patients at risk)
  - 1.5% of patients experienced their first infusion-related reaction during their third infusion (n=1144 patients at risk)
  - 0.6% of patients experienced their first infusion-related reaction during their fourth infusion (n=937 patients at risk)
  - 0.7% of patients experienced their first infusion-related reaction during their fifth infusion or a subsequent infusion (n=841 patients at risk)

MONITOR

Monitor patients for signs and symptoms of infusion-related reactions, including

Pyrexia	Chills	Flushing
Hypotension	Dyspnea	Wheezing
Back pain	Abdominal pain	Urticaria

- Premedicate with an antihistamine and with acetaminophen prior to the first 4 infusions of BAVENCIO and subsequently as needed

ASSESS

Assess the severity of the adverse reaction[13]

Grade 1	Grade 2	Grade 3	Grade 4
Mild transient reaction; infusion interruption is not indicated; intervention is not indicated	Therapy or infusion interruption is indicated but the reaction responds promptly to symptomatic treatment (eg, antihistamines, NSAIDs, narcotics, IV fluids); prophylactic medications are indicated for less than 24 hours	Prolonged (eg, not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae	Life-threatening consequences; urgent intervention indicated

MODIFY

Modify treatment based on severity

Grade 1-2	Grade 3-4
Interrupt or slow the rate of infusion	Stop the infusion and permanently discontinue BAVENCIO

*These data are from the JAVELIN Merkel 200 Trial and the JAVELIN Solid Tumor Trial.
IV=intravenous; NSAIDs=nonsteroidal anti-inflammatory drugs.

Please see Selected Safety Information throughout and full Prescribing Information here.

BAVENCIO® avelumab Injection 20 mg/mL

Complications of allogeneic hematopoietic stem cell transplantation

Clinical trial experience (across the development program)

- Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1 blocking antibody
- Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause)
- These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT

MONITOR — **Follow patients closely for evidence of transplant-related complications and intervene promptly**

ASSESS — **Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT**

PD-1=programmed death-1 receptor; PD-L1=programmed death ligand-1.

SELECTED SAFETY INFORMATION

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, ≥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, ≥20%) were fatigue, infusion-related reaction, musculoskeletal pain, nausea, decreased appetite, and urinary tract infection.

Selected laboratory abnormalities (all grades, ≥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 Selected Safety Information throughout and full Prescribing Information here.

BAVENCIO® avelumab Injection 20 mg/mL

CoverOne® patient support

CoverOne® provides patient access and reimbursement support services to help eligible patients* gain appropriate access to BAVENCIO® (avelumab)

*Eligibility requirements and restrictions may apply.

We recognize that each patient's situation is different, and are dedicated to helping eligible BAVENCIO patients one at a time

Please contact us at 1-844-8COVER1 if you have any questions.

CoverOne®

Call: 1-844-8COVER1
(1-844-826-8371)

Monday—Friday
8:00 AM—8:00 PM ET

Fax: 1-800-214-7295

Visit: CoverOne.com

Please have conversations with your patients about financing BAVENCIO so that they know all of the options that are available to them.

Patient discussion guide

It's important to check in with your patients about how they are doing with BAVENCIO® (avelumab)

The questions below are examples of conversation starters that can help you make sure your patients discuss any questions or concerns regarding their treatment.

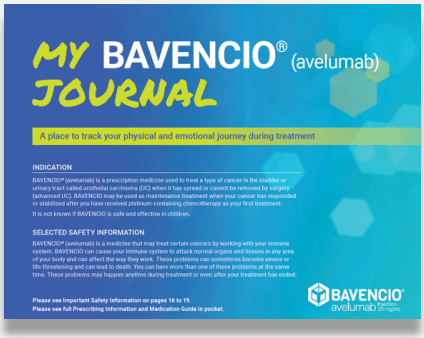
- **How are you feeling about your treatment?**
- **Do you have any questions about the side effects we discussed?**
- **Have you experienced any new or worsening signs or symptoms we discussed?**
- **Do you need assistance with insurance coverage or cost of treatment?**
- **Do you have any questions about your next infusion?**

Advise your patients that the adverse reactions listed in this guide are not all the possible side effects of treatment. Ask your patients to contact their cancer care team right away if they notice any signs or symptoms of adverse reactions. They may report side effects to FDA at 1-800-FDA-1088.

Patient education resources for BAVENCIO

You can access these resources on BAVENCIO.com, or you can ask your sales representative for hard copies

Patient Brochure



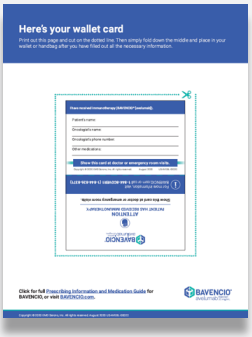
Patient Journal

Healthcare Provider Discussion Guide

Caregiver Guide

CoverOne® Patient Support Program Brochure

Maintenance Quick Reference Guide



Patient Wallet Card

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

BAVENCIO® avelumab Injection 20 mg/mL

Patient education resources for BAVENCIO

You can access these resources on BAVENCIO.com, or you can ask your sales representative

Explaining the Role of Maintenance Treatment

The **Patient Brochure**, **Maintenance Quick Reference Guide**, and the **Caregiver Guide** can be utilized to help explain the role and rationale of BAVENCIO maintenance therapy in metastatic urothelial carcinoma and includes Important Safety Information for BAVENCIO.

Understanding Immunotherapy

The **Patient Brochure** provides a brief patient-friendly explanation of the mechanism of action of BAVENCIO and how it works with the immune system to kill cancer cells; Important Safety Information for BAVENCIO is also included.

Discussing the JAVELIN Bladder 100 Trial

The **Patient Brochure** provides a summary of the study design and major efficacy results in the JAVELIN Bladder 100 Trial, as well as including Important Safety Information and information about possible side effects.

Reviewing Potential Side Effects and What to Watch for

The **Patient Brochure** and the **Caregiver Guide** provide Important Safety Information for BAVENCIO and discuss tips on how to manage certain side effects; the **Patient Journal** provides a place for patients to track their side effects, when they occurred, and their severity.

Discussing Reimbursement Support and Patient Assistance

The **CoverOne® Patient Support Program Brochure** can be utilized to discuss patient access and reimbursement support that may help eligible patients gain appropriate access to BAVENCIO.

Please see Selected Safety Information throughout and full Prescribing Information here.

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avelumab Injection 20 mg/mL

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed October 24, 2022. 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. **2.** von der Maase H, Sengelov L, Roberts JT, et al. Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patient with bladder cancer. *J Clin Oncol.* 2005;23(21):4602-4608. **3.** De Santis M, Bellmunt J, Mead G, et al. Randomized phase II/III trial assessing gemcitabine/carboplatin and methotrexate/carboplatin/vinblastine in patients with advanced urothelial cancer who are unfit for cisplatin-based chemotherapy: EORTC Study 30986. *J Clin Oncol.* 2012;30(2):191-199. **4.** Powles T, Park SH, Voog E, et al. Avelumab maintenance therapy for advanced or metastatic urothelial carcinoma. *N Engl J Med.* 2020;383(13):1218-1230. **5.** Cheeseman S, Thompson M, Sopwith W, et al. Current treatment and outcomes benchmark for locally advanced or metastatic urothelial cancer from a large UK-based single centre. *Front Oncol.* 2020;10(167). doi:10.3389/fonc.2020.00167. **6.** Galsky MD, Pal SK, Lin SW, et al. Real-world effectiveness of chemotherapy in elderly patients with metastatic bladder cancer in the United States. *Bladder Cancer.* 2018;4(2):227-238. **7.** Niegisch G, Gerullis H, Lin SW, et al. A real-world data study to evaluate treatment patterns, clinical characteristics and survival outcomes for first- and second-line treatment in locally advanced and metastatic urothelial cancer patients in Germany. *J Cancer.* 2018;9(8):1337-1348. **8.** Fisher M, Shenolikar R, Miller PJ, et al. Treatment patterns and outcomes in stage IV bladder cancer in a community oncology setting: 2008-2015. *Clin Genitourin Cancer.* 2018;16(6):e1171-e1179. **9.** Galsky MD, Hahn NM, Rosenberg J, et al. Treatment of patients with metastatic urothelial cancer "unfit" for cisplatin-based chemotherapy. *J Clin Oncol.* 2011;29(17):2432-2438. **10.** Aly A, Johnson C, Yang S, Botteman MF, Rao S, Hussain A. Overall survival, costs, and healthcare resource use by line of therapy in Medicare patients with newly diagnosed metastatic urothelial carcinoma. *J Med Econ.* 2019;22(7):662-670. **11.** Boyerinas B, Jochems C, Fantini M, et al. Antibody-dependent cellular cytotoxicity (ADCC) activity of a novel anti-PD-L1 antibody avelumab (MSB0010718C) on human tumor cells. *Cancer Immunol Res.* 2015;3(10):1148-1157. **12.** Data on file. Pfizer Inc., New York, NY. **13.** Common Terminology Criteria for Adverse Events (CTCAE), Version 5.0. US Dept. of Health and Human Services. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf. Accessed April 5, 2022.

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