



**PADCEV**<sup>®</sup>  
enfortumab vedotin-ejfv  
Injection for IV infusion 20 mg & 30 mg vials

# PADCEV<sup>®</sup> (enfortumab vedotin-ejfv) Order Set Resource

## BOXED WARNING: SERIOUS SKIN REACTIONS

- PADCEV can cause severe and fatal cutaneous adverse reactions including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), which occurred predominantly during the first cycle of treatment, but may occur later.
- Closely monitor patients for skin reactions.
- Immediately withhold PADCEV and consider referral for specialized care for suspected SJS or TEN or severe skin reactions.
- Permanently discontinue PADCEV in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions.

## Indication

PADCEV<sup>®</sup>, in combination with pembrolizumab, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC).

PADCEV, as a single agent, is indicated for the treatment of adult patients with locally advanced or mUC who:

- have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum-containing chemotherapy, or
- are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.





This document details information about PADCEV and PADCEV in combination with pembrolizumab, such as the indication, cycle information, treatment calendar, important dosing information and dosing modifications; however, the information contained in this document is not fully inclusive of all details of the PADCEV Prescribing Information. The clinical data elements are suggestions only. The customer must determine the final elements to include in line with the organization’s expectations, goals and electronic health record (EHR) governing principles. The customers (ie, physician, medical group, integrated delivery network [IDN]) shall be solely responsible for implementation, testing and monitoring of the instructions to ensure proper orientation in each customer’s EHR system.

While EHRs may assist providers in identifying appropriate patients for consideration of assessment and treatment, the decision and action should ultimately be made by a provider in consultation with the patient after a review of the patient’s records to determine eligibility, and Astellas and Seagen shall have no liability thereto.

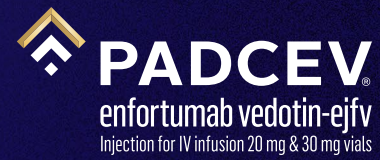
Please consult the most recent version of the PADCEV Prescribing Information for full medication details. The most recent version of the PADCEV Prescribing Information may be found at: [https://astellas.us/docs/PADCEV\\_label.pdf](https://astellas.us/docs/PADCEV_label.pdf).

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# Indication and Important Safety Information



Indication and ISI

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### Indication

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- are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

## IMPORTANT SAFETY INFORMATION

### Warnings and Precautions

**Skin reactions** Severe cutaneous adverse reactions, including fatal cases of SJS or TEN occurred in patients treated with PADCEV. SJS and TEN occurred predominantly during the first cycle of treatment but may occur later. Skin reactions occurred in 70% (all grades) of the 564 patients treated with PADCEV in combination with pembrolizumab in clinical trials. When PADCEV was given in combination with pembrolizumab, the incidence of skin reactions, including severe events, occurred at a higher rate compared to PADCEV as a single agent. The majority of the skin reactions that occurred with combination therapy included maculo-papular rash, macular rash and papular rash. Grade 3-4 skin reactions occurred in 17% of patients (Grade 3: 16%, Grade 4: 1%), including maculo-papular rash, bullous dermatitis, dermatitis, exfoliative dermatitis, pemphigoid, rash, erythematous rash, macular rash, and papular rash. A fatal reaction of bullous dermatitis occurred in one patient (0.2%). The median time to onset of severe skin reactions was 1.7 months (range: 0.1 to 17.2 months). Skin reactions led to discontinuation of PADCEV in 6% of patients.

Skin reactions occurred in 58% (all grades) of the 720 patients treated with PADCEV as a single agent in clinical trials. Twenty-three percent (23%) of patients had maculo-papular rash and 34% had pruritus. Grade 3-4 skin reactions occurred in 14% of patients, including maculo-papular rash, erythematous rash, rash or drug eruption, symmetrical drug-related intertriginous and flexural exanthema (SDRIFE), bullous dermatitis, exfoliative dermatitis, and palmar-plantar erythrodysesthesia. The median time to onset of severe skin reactions was 0.6 months (range: 0.1 to 8 months). Among patients experiencing a skin reaction leading to dose interruption who then restarted PADCEV (n=75), 24% of patients restarting at the same dose and 24% of patients restarting at a reduced dose experienced recurrent severe skin reactions. Skin reactions led to discontinuation of PADCEV in 3.1% of patients.

Monitor patients closely throughout treatment for skin reactions. Consider topical corticosteroids and antihistamines, as clinically indicated. For persistent or recurrent Grade 2 skin reactions, consider withholding PADCEV until Grade ≤1. Withhold PADCEV and refer for specialized care for suspected SJS, TEN or for Grade 3 skin reactions. Permanently discontinue PADCEV in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions.

Patient Counseling

Care Team Considerations

Safety

Lab Parameters

Clinical Verification

Drug-Drug Interactions

Dosing and Administration

Helpful Links



## IMPORTANT SAFETY INFORMATION (cont'd)

### Warnings and Precautions (cont'd)

**Hyperglycemia and diabetic ketoacidosis (DKA)**, including fatal events, occurred in patients with and without pre-existing diabetes mellitus, treated with PADCEV. Patients with baseline hemoglobin A1C  $\geq 8\%$  were excluded from clinical trials. In clinical trials of PADCEV as a single agent, 17% of the 720 patients treated with PADCEV developed hyperglycemia of any grade; 7% of patients developed Grade 3-4 hyperglycemia (Grade 3: 6.5%, Grade 4: 0.6%). Fatal events of hyperglycemia and DKA occurred in one patient each (0.1%). The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher body mass index and in patients with higher baseline A1C. The median time to onset of hyperglycemia was 0.5 months (range: 0 to 20 months). Hyperglycemia led to discontinuation of PADCEV in 0.7% of patients. Five percent (5%) of patients required initiation of insulin therapy for treatment of hyperglycemia. Of the patients who initiated insulin therapy for treatment of hyperglycemia, 66% (23/35) discontinued insulin at the time of last evaluation. Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia. If blood glucose is elevated ( $>250$  mg/dL), withhold PADCEV.

**Pneumonitis/Interstitial Lung Disease (ILD)** Severe, life-threatening or fatal pneumonitis/ILD occurred in patients treated with PADCEV. When PADCEV was given in combination with pembrolizumab, 10% of the 564 patients treated with combination therapy had pneumonitis/ILD of any grade and 4% had Grade 3-4. A fatal event of pneumonitis/ILD occurred in two patients (0.4%). The incidence of pneumonitis/ILD, including severe events, occurred at a higher rate when PADCEV was given in combination with pembrolizumab compared to PADCEV as a single agent. The median time to onset of any grade pneumonitis/ILD was 4 months (range: 0.3 to 26 months).

In clinical trials of PADCEV as a single agent, 3% of the 720 patients treated with PADCEV had pneumonitis/ILD of any grade and 0.8% had Grade 3-4. The median time to onset of any grade pneumonitis/ILD was 2.9 months (range: 0.6 to 6 months).

Monitor patients for signs and symptoms indicative of pneumonitis/ILD such as hypoxia, cough, dyspnea or interstitial infiltrates on radiologic exams. Evaluate and exclude infectious, neoplastic and other causes for such signs and symptoms through appropriate investigations. Withhold PADCEV for patients who develop

Grade 2 pneumonitis/ILD and consider dose reduction. Permanently discontinue PADCEV in all patients with Grade 3 or 4 pneumonitis/ILD.

**Peripheral neuropathy (PN)** When PADCEV was given in combination with pembrolizumab, 67% of the 564 patients treated with combination therapy had PN of any grade, 36% had Grade 2 neuropathy, and 7% had Grade 3 neuropathy. The incidence of PN occurred at a higher rate when PADCEV was given in combination with pembrolizumab compared to PADCEV as a single agent. The median time to onset of Grade  $\geq 2$  PN was 6 months (range: 0.3 to 25 months).

PN occurred in 53% of the 720 patients treated with PADCEV as a single agent in clinical trials including 38% with sensory neuropathy, 8% with muscular weakness and 7% with motor neuropathy. Thirty percent of patients experienced Grade 2 reactions and 5% experienced Grade 3-4 reactions. PN occurred in patients treated with PADCEV with or without preexisting PN. The median time to onset of Grade  $\geq 2$  PN was 4.9 months (range: 0.1 to 20 months). Neuropathy led to treatment discontinuation in 6% of patients.

Monitor patients for symptoms of new or worsening PN and consider dose interruption or dose reduction of PADCEV when PN occurs. Permanently discontinue PADCEV in patients who develop Grade  $\geq 3$  PN.

**Ocular disorders** were reported in 40% of the 384 patients treated with PADCEV as a single agent in clinical trials in which ophthalmologic exams were scheduled. The majority of these events involved the cornea and included events associated with dry eye such as keratitis, blurred vision, increased lacrimation, conjunctivitis, limbal stem cell deficiency, and keratopathy. Dry eye symptoms occurred in 30% of patients, and blurred vision occurred in 10% of patients, during treatment with PADCEV. The median time to onset to symptomatic ocular disorder was 1.7 months (range: 0 to 30.6 months). Monitor patients for ocular disorders. Consider artificial tears for prophylaxis of dry eyes and ophthalmologic evaluation if ocular symptoms occur or do not resolve. Consider treatment with ophthalmic topical steroids, if indicated after an ophthalmic exam. Consider dose interruption or dose reduction of PADCEV for symptomatic ocular disorders.



## IMPORTANT SAFETY INFORMATION (cont'd)

### Warnings and Precautions (cont'd)

**Infusion site extravasation** Skin and soft tissue reactions secondary to extravasation have been observed after administration of PADCEV. Of the 720 patients treated with PADCEV as a single agent in clinical trials, 1% of patients experienced skin and soft tissue reactions, including 0.3% who experienced Grade 3-4 reactions. Reactions may be delayed. Erythema, swelling, increased temperature, and pain worsened until 2-7 days after extravasation and resolved within 1-4 weeks of peak. Two patients (0.3%) developed extravasation reactions with secondary cellulitis, bullae, or exfoliation. Ensure adequate venous access prior to starting PADCEV and monitor for possible extravasation during administration. If extravasation occurs, stop the infusion and monitor for adverse reactions.

**Embryo-fetal toxicity** PADCEV can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during PADCEV treatment and for 2 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with PADCEV and for 4 months after the last dose.

### ADVERSE REACTIONS

**Most common adverse reactions, including laboratory abnormalities ( $\geq 20\%$ ) (PADCEV in combination with pembrolizumab)** Increased aspartate aminotransferase (AST), increased creatinine, rash, increased glucose, PN, increased lipase, decreased lymphocytes, increased alanine aminotransferase (ALT), decreased hemoglobin, fatigue, decreased sodium, decreased phosphate, decreased albumin, pruritus, diarrhea, alopecia, decreased weight, decreased appetite, increased urate, decreased neutrophils, decreased potassium, dry eye, nausea, constipation, increased potassium, dysgeusia, urinary tract infection and decreased platelets.

**Most common adverse reactions, including laboratory abnormalities ( $\geq 20\%$ ) (PADCEV monotherapy)** Increased glucose, increased AST, decreased lymphocytes, increased creatinine, rash, fatigue, PN, decreased albumin, decreased hemoglobin, alopecia, decreased appetite, decreased neutrophils, decreased sodium, increased ALT, decreased phosphate, diarrhea, nausea, pruritus, increased urate, dry eye, dysgeusia, constipation, increased lipase, decreased weight, decreased platelets, abdominal pain, dry skin.

### EV-302 Study: 440 patients with previously untreated la/mUC (PADCEV in combination with pembrolizumab)

**Serious adverse reactions** occurred in 50% of patients treated with PADCEV in combination with pembrolizumab. The most common serious adverse reactions ( $\geq 2\%$ ) were rash (6%), acute kidney injury (5%), pneumonitis/ILD (4.5%), urinary tract infection (3.6%), diarrhea (3.2%), pneumonia (2.3%), pyrexia (2%), and hyperglycemia (2%). **Fatal adverse reactions** occurred in 3.9% of patients treated with PADCEV in combination with pembrolizumab including acute respiratory failure (0.7%), pneumonia (0.5%), and pneumonitis/ILD (0.2%).

Adverse reactions leading to discontinuation of PADCEV occurred in 35% of patients. The **most common adverse reactions ( $\geq 2\%$ ) leading to discontinuation** of PADCEV were PN (15%), rash (4.1%) and pneumonitis/ILD (2.3%). Adverse reactions leading to dose interruption of PADCEV occurred in 73% of patients. The **most common adverse reactions ( $\geq 2\%$ ) leading to dose interruption** of PADCEV were PN (22%), rash (16%), COVID-19 (10%), diarrhea (5%), pneumonitis/ILD (4.8%), fatigue (3.9%), hyperglycemia (3.6%), increased ALT (3%) and pruritus (2.5%). Adverse reactions leading to dose reduction of PADCEV occurred in 42% of patients. The **most common adverse reactions ( $\geq 2\%$ ) leading to dose reduction** of PADCEV were rash (16%), PN (13%) and fatigue (2.7%).



## IMPORTANT SAFETY INFORMATION (cont'd)

### ADVERSE REACTIONS (cont'd)

**EV-103 Study: 121 patients with previously untreated la/mUC who were not eligible for cisplatin-containing chemotherapy (PADCEV in combination with pembrolizumab)**

**Serious adverse reactions** occurred in 50% of patients treated with PADCEV in combination with pembrolizumab; the most common ( $\geq 2\%$ ) were acute kidney injury (7%), urinary tract infection (7%), urosepsis (5%), sepsis (3.3%), pneumonia (3.3%), hematuria (3.3%), pneumonitis/ILD (3.3%), urinary retention (2.5%), diarrhea (2.5%), myasthenia gravis (2.5%), myositis (2.5%), anemia (2.5%), and hypotension (2.5%). **Fatal adverse reactions** occurred in 5% of patients treated with PADCEV in combination with pembrolizumab, including sepsis (1.6%), bullous dermatitis (0.8%), myasthenia gravis (0.8%), and pneumonitis/ILD (0.8%). **Adverse reactions leading to discontinuation** of PADCEV occurred in 36% of patients; the most common ( $\geq 2\%$ ) were PN (20%) and rash (6%). **Adverse reactions leading to dose interruption** of PADCEV occurred in 69% of patients; the most common ( $\geq 2\%$ ) were PN (18%), rash (12%), increased lipase (6%), pneumonitis/ILD (6%), diarrhea (4.1%), acute kidney injury (3.3%), increased ALT (3.3%), fatigue (3.3%), neutropenia (3.3%), urinary tract infection (3.3%), increased amylase (2.5%), anemia (2.5%), COVID-19 (2.5%), hyperglycemia (2.5%), and hypotension (2.5%). **Adverse reactions leading to dose reduction** of PADCEV occurred in 45% of patients; the most common ( $\geq 2\%$ ) were PN (17%), rash (12%), fatigue (5%), neutropenia (5%), and diarrhea (4.1%).

**EV-301 Study: 296 patients previously treated with a PD-1/L1 inhibitor and platinum-based chemotherapy (PADCEV monotherapy)**

**Serious adverse reactions** occurred in 47% of patients treated with PADCEV; the most common ( $\geq 2\%$ ) were urinary tract infection, acute kidney injury (7% each), and pneumonia (5%). **Fatal adverse reactions** occurred in 3% of patients, including multiorgan dysfunction (1%), hepatic dysfunction, septic shock, hyperglycemia, pneumonitis/ILD, and pelvic abscess (0.3% each). **Adverse reactions leading to discontinuation** occurred in 17% of patients; the most common ( $\geq 2\%$ ) were PN (5%) and rash (4%). **Adverse reactions leading to dose interruption** occurred in 61% of patients; the most common ( $\geq 4\%$ ) were PN (23%), rash (11%), and fatigue (9%). **Adverse reactions leading to dose reduction** occurred in 34% of patients; the most common ( $\geq 2\%$ ) were PN (10%), rash (8%), decreased appetite, and fatigue (3% each).

**EV-201, Cohort 2 Study: 89 patients previously treated with a PD-1/L1 inhibitor and not eligible for cisplatin-based chemotherapy (PADCEV monotherapy)**

**Serious adverse reactions** occurred in 39% of patients treated with PADCEV; the most common ( $\geq 3\%$ ) were pneumonia, sepsis, and diarrhea (5% each). **Fatal adverse reactions** occurred in 8% of patients, including acute kidney injury (2.2%), metabolic acidosis, sepsis, multiorgan dysfunction, pneumonia, and pneumonitis/ILD (1.1% each). **Adverse reactions leading to discontinuation** occurred in 20% of patients; the most common ( $\geq 2\%$ ) was PN (7%). **Adverse reactions leading to dose interruption** occurred in 60% of patients; the most common ( $\geq 3\%$ ) were PN (19%), rash (9%), fatigue (8%), diarrhea (5%), increased AST, and hyperglycemia (3% each). **Adverse reactions leading to dose reduction** occurred in 49% of patients; the most common ( $\geq 3\%$ ) were PN (19%), rash (11%), and fatigue (7%).

### DRUG INTERACTIONS

**Effects of other drugs on PADCEV (Dual P-gp and Strong CYP3A4 Inhibitors)**

Concomitant use with dual P-gp and strong CYP3A4 inhibitors may increase unconjugated monomethyl auristatin E exposure, which may increase the incidence or severity of PADCEV toxicities. Closely monitor patients for signs of toxicity when PADCEV is given concomitantly with dual P-gp and strong CYP3A4 inhibitors.

### SPECIFIC POPULATIONS

**Lactation** Advise lactating women not to breastfeed during treatment with PADCEV and for 3 weeks after the last dose.

**Hepatic impairment** Avoid the use of PADCEV in patients with moderate or severe hepatic impairment.

**Please see full Prescribing Information, including BOXED WARNING FOR SERIOUS SKIN REACTIONS.**



Consider discussing with patients that dose modifications and/or discontinuations may be necessary to treat the following adverse reactions [see *Dose Modifications*]

- **Dose Reductions**

- Dose reductions may be required. Efficacy results from clinical trials with PADCEV reflect full and modified dosing regimens

- **Skin Reactions**

- Inform patients that severe skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) with fatal outcomes have occurred after administration of PADCEV, predominantly during the first cycle of treatment but may occur later
- Advise patients to contact their healthcare provider (HCP) immediately if they develop new target lesions (skin reactions that look like rings), rash or itching that continues to get worse, progressively worsening skin reactions, blistering or peeling of the skin, painful sores or ulcers in the mouth/nose/throat/genital area, fever or flu-like symptoms or swollen lymph nodes [see *Boxed Warning and Warnings and Precautions*]
- It is important to reiterate that patients should contact their HCP immediately if they develop skin reactions and they should follow provider guidance

- **Hyperglycemia**

- Inform patients about the risk of hyperglycemia and how to recognize associated symptoms including frequent urination, increased thirst, blurred vision, confusion, drowsiness, loss of appetite, fruity smell on breath, nausea/vomiting/stomach pain or increased difficulty controlling blood sugar [see *Warnings and Precautions*]

- **Pneumonitis/Interstitial Lung Disease (ILD)**

- Advise patients to immediately report new or worsening respiratory symptoms, including shortness of breath, cough or trouble breathing [see *Warnings and Precautions*]

- **Peripheral Neuropathy**

- Inform patients to immediately report to their HCP any onset of numbness and tingling of the hands or feet or muscle weakness [see *Warnings and Precautions*]

- **Ocular Disorders**

- Advise patients to contact their HCP if they experience any visual changes such as dry eyes, increased tearing or blurred vision [see *Warnings and Precautions*]. In order to prevent or treat dry eyes, consider advising patients to use artificial tear substitutes

- **Infusion Site Extravasation**

- Inform patients that infusion site reactions have occurred after administration of PADCEV. These reactions generally occurred immediately after administration but, in some instances, had a delayed onset (eg, 24 hours). Instruct patients to contact their HCP immediately if they experience any signs of an infusion site reaction including any redness, swelling, itching, blister, peeling skin or discomfort at the infusion site



## Additional Safety Considerations

- **Reproductive Health**

- Advise appropriate patients (pregnant women, female and male patients of reproductive potential) of the potential risk to the fetus and the risk of impairment to fertility. Advise female patients of reproductive potential to inform their HCPs of a known or suspected pregnancy and to use effective contraception during treatment with PADCEV and for 2 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with PADCEV and for 4 months after the last dose

- **Lactation**

- Advise women not to breastfeed during treatment with PADCEV and for 3 weeks after the last dose

- **Infertility**

- Advise females and males of reproductive potential that PADCEV may impair fertility





## Prior to Initiation of PADCEV



Check your local or institutional guidelines for antiemetic use for treating patients with cancer

- Consider artificial tears for patients as prophylaxis for dry eyes



Monitor patients for ocular disorders. Consider artificial tears for prophylaxis of dry eyes and ophthalmologic evaluation if ocular symptoms occur or do not resolve. Consider treatment with ophthalmic topical steroids, if indicated after an ophthalmic exam

- Provide patient counseling information to patients (on page 7)



Consider discussing potential adverse reactions patients may anticipate and how they can be treated

- Consider screening patients for social determinants of health

## Adverse Events During Treatment With PADCEV

### • Skin Reactions

- Monitor patients closely throughout treatment for skin reactions



Consider topical corticosteroids and antihistamines, as clinically indicated

### • Pneumonitis/ILD

- Monitor patients for signs and symptoms indicative of pneumonitis/ILD such as hypoxia, cough, dyspnea or interstitial infiltrates on radiologic exams. Evaluate and exclude infectious, neoplastic and other causes for such signs and symptoms through appropriate investigations

### • Peripheral Neuropathy

- Inform patients to report to their HCP any numbness and tingling of the hands or feet or muscle weakness

### • Hyperglycemia

- Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia



Consider providing glucose testing supplies for patients, as appropriate

### • Infusion Site Extravasation

- Ensure adequate venous access prior to starting PADCEV and monitor for possible extravasation during administration. If extravasation occurs, stop the infusion and monitor for adverse reactions



## Most Common Adverse Reactions, Including Laboratory Abnormalities, (≥20%) Reported with PADCEV for Monitoring Consideration

Adverse reactions and laboratory abnormalities are listed in order of highest to lowest occurrence, according to the Prescribing Information

### Categories of Safety

#### Adverse Reactions

- Skin and subcutaneous tissue disorders
- Nervous system disorders
- Metabolism and nutrition disorders
- Gastrointestinal disorders
- General disorders and administration site conditions
- Weight changes
- Eye disorders
- Infections and infestations

#### Laboratory Abnormalities

- Hematology
- Chemistry

### PADCEV at 1.25 mg/kg in combination with pembrolizumab (based on 564 patients in EV-302 and EV-103):

#### Adverse Reactions

<span style="color: red;">■</span> Rash
<span style="color: orange;">■</span> Peripheral neuropathy
<span style="color: grey;">■</span> Fatigue
<span style="color: red;">■</span> Pruritus
<span style="color: blue;">■</span> Diarrhea
<span style="color: red;">■</span> Alopecia
<span style="color: purple;">■</span> Decreased weight
<span style="color: green;">■</span> Decreased appetite
<span style="color: brown;">■</span> Dry eye
<span style="color: blue;">■</span> Nausea
<span style="color: blue;">■</span> Constipation
<span style="color: orange;">■</span> Dysgeusia
<span style="color: pink;">■</span> Urinary tract infection

#### Laboratory Abnormalities

<span style="color: black;">■</span> Increased AST
<span style="color: black;">■</span> Increased creatinine
<span style="color: black;">■</span> Increased glucose
<span style="color: black;">■</span> Increased lipase
<span style="color: purple;">■</span> Decreased lymphocytes
<span style="color: black;">■</span> Increased ALT
<span style="color: purple;">■</span> Decreased hemoglobin
<span style="color: black;">■</span> Decreased sodium
<span style="color: black;">■</span> Decreased phosphate
<span style="color: black;">■</span> Decreased albumin
<span style="color: black;">■</span> Increased urate
<span style="color: purple;">■</span> Decreased neutrophils
<span style="color: black;">■</span> Decreased potassium
<span style="color: black;">■</span> Increased potassium
<span style="color: purple;">■</span> Decreased platelets

### PADCEV as a single agent at 1.25 mg/kg (based on a pooled population of 720 patients in EV-301, EV-201, EV-203, EV-101 and EV-102):

#### Adverse Reactions

<span style="color: red;">■</span> Rash
<span style="color: grey;">■</span> Fatigue
<span style="color: orange;">■</span> Peripheral neuropathy
<span style="color: red;">■</span> Alopecia
<span style="color: green;">■</span> Decreased appetite
<span style="color: blue;">■</span> Diarrhea
<span style="color: blue;">■</span> Nausea
<span style="color: red;">■</span> Pruritus
<span style="color: brown;">■</span> Dry eye
<span style="color: orange;">■</span> Dysgeusia
<span style="color: blue;">■</span> Constipation
<span style="color: purple;">■</span> Decreased weight
<span style="color: blue;">■</span> Abdominal pain
<span style="color: red;">■</span> Dry skin

#### Laboratory Abnormalities

<span style="color: black;">■</span> Increased glucose
<span style="color: black;">■</span> Increased AST
<span style="color: purple;">■</span> Decreased lymphocytes
<span style="color: black;">■</span> Increased creatinine
<span style="color: black;">■</span> Decreased albumin
<span style="color: purple;">■</span> Decreased hemoglobin
<span style="color: purple;">■</span> Decreased neutrophils
<span style="color: black;">■</span> Decreased sodium
<span style="color: black;">■</span> Increased ALT
<span style="color: black;">■</span> Decreased phosphate
<span style="color: black;">■</span> Increased urate
<span style="color: black;">■</span> Increased lipase
<span style="color: purple;">■</span> Decreased platelets

ALT, alanine aminotransferase; AST, aspartate aminotransferase



## Comprehensive Metabolic Panel

- **Glucose**

- Insert institutional lab parameter as EHR capabilities allow
- Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia. Withhold PADCEV if blood glucose is >250 mg/dL
- The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher body mass index and in patients with higher baseline A1C

- **Hepatic Impairment**

- Insert institutional lab parameters as EHR capabilities allow
- Total bilirubin and AST/ALT:
  - Avoid the use of PADCEV in patients with moderate or severe hepatic impairment (total bilirubin >1.5 × upper limit of normal [ULN] and AST any)

## Hematology: Complete Blood Counts With Differential

- Insert institutional lab parameters as EHR capabilities allow
- Recommended dose modifications for PADCEV for adverse reactions of hematologic toxicity:
  - Grade 3, or Grade 2 thrombocytopenia: Withhold until Grade ≤1, then resume treatment at the same dose level or consider dose reduction by 1 dose level
  - Grade 4: Withhold until Grade ≤1, then reduce dose by 1 dose level or discontinue treatment
  - See dose modification guidance on page 16



## Nursing Verification

- Assess patient for all adverse reactions during the course of treatment
- Monitor lab parameters

## Pharmacist Verification

- Verify order indication and dosing:
  - **PADCEV in combination with pembrolizumab**
    - Indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC)
    - PADCEV dosing regimen
      - Intravenous infusion: 1.25 mg/kg (maximum of 125 mg for patients  $\geq 100$  kg)
      - Administer over 30 minutes on Days 1 and 8
      - 21-day cycle
  - **PADCEV as a single agent**
    - Indicated for adult patients with locally advanced/mUC who:
      - Have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum-containing chemotherapy, or
      - Are ineligible for cisplatin-containing chemotherapy and have previously received 1 or more prior lines of therapy
    - PADCEV dosing regimen
      - Intravenous infusion: 1.25 mg/kg (maximum of 125 mg for patients  $\geq 100$  kg)
      - Administer over 30 minutes on Days 1, 8 and 15
      - 28-day cycle
  - For both regimens, continue until disease progression or unacceptable toxicity. Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab

### PADCEV Dosage Reduction Schedule for Adverse Reactions

Starting dose	1.25 mg/kg up to 125 mg
First dose reduction	1.0 mg/kg up to 100 mg
Second dose reduction	0.75 mg/kg up to 75 mg
Third dose reduction	0.5 mg/kg up to 50 mg

- Visually inspect the infusion bag for any particulate matter or discoloration prior to use. The reconstituted solution should be clear to slightly opalescent, colorless to light yellow and free of visible particles. Do not use the infusion bag if particulate matter or discoloration is observed
- Ensure safe handling of hazardous medications per institutional policies
- See dose modification guidance on page 16



# Drug-Drug Interactions (DDI)



Consider DDI checks per institutional policy and guidelines (to add alert or as medication rule).  
Recommend running a DDI check prior to treatment

- **Dual P-glycoprotein (P-gp) and Strong CYP3A4 Inhibitors**

- Concomitant use with dual P-gp and strong CYP3A4 inhibitors may increase unconjugated monomethyl auristatin E (MMAE) exposure, which may increase the incidence or severity of PADCEV toxicities. Closely monitor patients for signs of toxicity when PADCEV is given concomitantly with dual P-gp and strong CYP3A4 inhibitors



# Dosing and Administration

## Recommended Dosing

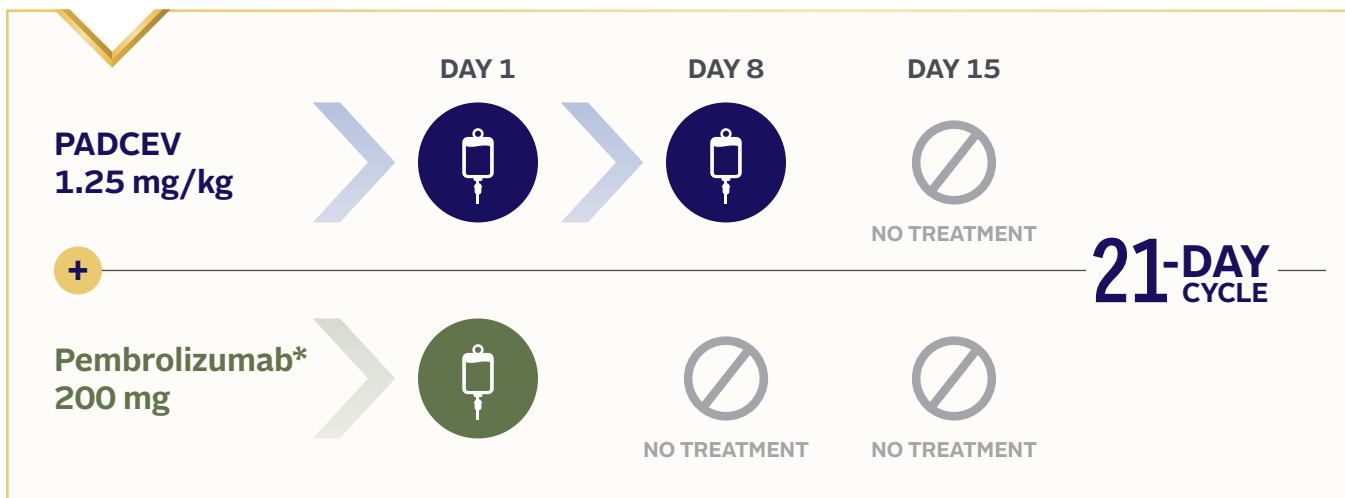
### PADCEV in combination with pembrolizumab

- When given in combination with pembrolizumab, the recommended dose of PADCEV is 1.25 mg/kg (up to a maximum of 125 mg for patients  $\geq 100$  kg) administered as an intravenous infusion over 30 minutes on Days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity. Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab



Consider adding your preferred EHR functionality (eg, radio buttons, check boxes, drop downs, artificial intelligence) to support patient dose reduction, when needed

### PADCEV + PEMBROLIZUMAB COMBINATION DOSING IN THE EV-302 TRIAL



\*Refer to the pembrolizumab Prescribing Information for the recommended dosing information. In clinical trials conducted with PADCEV and pembrolizumab, pembrolizumab was infused 30 minutes after completion of PADCEV infusion.

### PADCEV as a single agent

- The recommended dose of PADCEV as a single agent is 1.25 mg/kg (up to a maximum dose of 125 mg for patients  $\geq 100$  kg) given as an intravenous infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity

### PADCEV DOSING AS A SINGLE AGENT





## Example Dosing Calendar

### 21-DAY CYCLE PADCEV + PEMBROLIZUMAB COMBINATION DOSING IN THE EV-302 TRIAL

<b>WEEK 1</b>	DAY 1 	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
<b>WEEK 2</b>	DAY 8 	DAY 9	DAY 10	DAY 11	DAY 12	DAY 13	DAY 14
<b>WEEK 3</b>	DAY 15	DAY 16	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21

PADCEV 1.25 mg/kg    Pembrolizumab\* 200 mg

### 28-DAY CYCLE PADCEV DOSING AS A SINGLE AGENT

<b>WEEK 1</b>	DAY 1 	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
<b>WEEK 2</b>	DAY 8 	DAY 9	DAY 10	DAY 11	DAY 12	DAY 13	DAY 14
<b>WEEK 3</b>	DAY 15 	DAY 16	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21
<b>WEEK 4</b>	DAY 22	DAY 23	DAY 24	DAY 25	DAY 26	DAY 27	DAY 28

PADCEV 1.25 mg/kg

\*Refer to the pembrolizumab Prescribing Information for the recommended dosing information.



# Dosing and Administration (cont'd)

Dose Modifications		
Adverse Reaction	Severity*	Dose Modification*
<b>Skin reactions</b> [see Boxed Warning, Warnings and Precautions]	For persistent or recurrent Grade 2 skin reactions	Consider withholding until Grade $\leq 1$ , then resume treatment at the same dose level or dose reduce by 1 dose level.
	Grade 3 skin reactions	Withhold until Grade $\leq 1$ , then resume treatment at the same dose level or dose reduce by 1 dose level.
	Suspected SJS or TEN	Immediately withhold, consult a specialist to confirm the diagnosis. If not SJS/TEN, see Grade 2-4 skin reactions.
	Confirmed SJS or TEN; Grade 4 or recurrent Grade 3 skin reactions	Permanently discontinue.
<b>Hyperglycemia</b> [see Warnings and Precautions]	Blood glucose $>250$ mg/dL	Withhold until elevated blood glucose has improved to $\leq 250$ mg/dL, then resume treatment at the same dose level.
<b>Pneumonitis/ILD</b> [see Warnings and Precautions]	Grade 2	Withhold until Grade $\leq 1$ , then resume treatment at the same dose level or consider dose reduction by 1 dose level.
	Grade $\geq 3$	Permanently discontinue.
<b>Peripheral neuropathy</b> [see Warnings and Precautions]	Grade 2	Withhold until Grade $\leq 1$ , then resume treatment at the same dose level (if first occurrence). For a recurrence, withhold until Grade $\leq 1$ , then resume treatment reduced by 1 dose level.
	Grade $\geq 3$	Permanently discontinue.
<b>Other nonhematologic toxicity</b> [see Adverse Reactions]	Grade 3	Withhold until Grade $\leq 1$ , then resume treatment at the same dose level or consider dose reduction by 1 dose level.
	Grade 4	Permanently discontinue.
<b>Hematologic toxicity</b> [see Adverse Reactions]	Grade 3, or Grade 2 thrombocytopenia	Withhold until Grade $\leq 1$ , then resume treatment at the same dose level or consider dose reduction by 1 dose level.
	Grade 4	Withhold until Grade $\leq 1$ , then reduce dose by 1 dose level or discontinue treatment.

\*Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, Grade 4 is life-threatening.





## Dosing and Administration (cont'd)

### Dosage Reduction Schedule

Starting dose	1.25 mg/kg up to 125 mg
First dose reduction	1.0 mg/kg up to 100 mg
Second dose reduction	0.75 mg/kg up to 75 mg
Third dose reduction	0.5 mg/kg up to 50 mg

### Dosage Forms and Strengths

- For injection: PADCEV 20 mg and 30 mg are supplied as a sterile, preservative-free, white to off-white lyophilized powder in single-dose vials for reconstitution. PADCEV vials are available in the following packages:
  - Carton of one 20 mg single-dose vial (NDC 51144-020-01)
  - Carton of one 30 mg single-dose vial (NDC 51144-030-01)

#### 20 mg vial



#### 30 mg vial



### Administration and Handling Highlights

- See full Prescribing Information for details
  - Administer PADCEV as an intravenous infusion only.
  - Prior to administration, the PADCEV vial is reconstituted with sterile water for injection (SWFI). The reconstituted solution is subsequently diluted in an intravenous infusion bag containing either 5% dextrose injection, USP; 0.9% sodium chloride injection, USP; or lactated Ringer's injection, USP
  - The infusion bag size should allow enough diluent to achieve a final concentration of 0.3 mg/mL to 4 mg/mL PADCEV
  - PADCEV is a hazardous drug. Follow applicable special handling and disposal procedures by your institution or refer to Occupational Safety and Health Administration guidance found here: <http://www.osha.gov/SLTC/hazardousdrugs/index.html>



In clinical trials conducted with PADCEV and pembrolizumab, pembrolizumab was infused 30 minutes after completion of PADCEV infusion



## Helpful Links

- PADCEV Prescribing Information: [https://astellas.us/docs/PADCEV\\_label.pdf](https://astellas.us/docs/PADCEV_label.pdf)
- PADCEV Patient Information: [https://astellas.us/docs/PADCEV\\_label.pdf#page=29](https://astellas.us/docs/PADCEV_label.pdf#page=29)
- Patient Education Resources: <https://www.padcev.com/caregiver-tips>
- PADCEV Support Solutions<sup>SM</sup> Website: <https://astellaspharmassupportsolutions.com/patient/padcev/index.aspx>
- PADCEV HCP Website: <https://www.padcev.com/hcp>
- HCP Support Materials: <https://www.padcev.com/hcp/resources>
- EV-301 Study Protocol: [https://www.nejm.org/doi/suppl/10.1056/NEJMoa2035807/suppl\\_file/nejmoa2035807\\_protocol.pdf](https://www.nejm.org/doi/suppl/10.1056/NEJMoa2035807/suppl_file/nejmoa2035807_protocol.pdf)
- EV-201 Study Protocol: [https://ascopubs.org/doi/suppl/10.1200/JCO.19.01140/suppl\\_file/protocol\\_jco.19.01140.pdf](https://ascopubs.org/doi/suppl/10.1200/JCO.19.01140/suppl_file/protocol_jco.19.01140.pdf)
- EV-103 Study Protocol: [https://ascopubs.org/doi/suppl/10.1200/JCO.22.01643/suppl\\_file/protocol\\_JCO.22.01643.pdf](https://ascopubs.org/doi/suppl/10.1200/JCO.22.01643/suppl_file/protocol_JCO.22.01643.pdf)
- EV-302 Clinical Trial: <https://clinicaltrials.gov/study/NCT04223856>

**Reference:** PADCEV [package insert]. Northbrook, IL: Astellas Pharma US, Inc.



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