MIBC

PADCEV® DOSING AND ADMINISTRATION

POCKET GUIDE

For muscle-invasive bladder cancer (MIBC) treatment regardless of cisplatin eligibility[1]

PADCEV J-code J9177

This information is provided for educational purposes only. This is not a guarantee of reimbursement.
It is the provider's responsibility to determine the appropriate code and to submit true and correct claims.

BOXED WARNING: SERIOUS SKIN REACTIONS

- **PADCEV (enfortumab vedotin-ejfv) 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, in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph, as neoadjuvant treatment and then continued after cystectomy as adjuvant treatment, is indicated for the treatment of adult patients with muscle invasive bladder cancer (MIBC).

PERIOPERATIVE

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

+ pembrolizumab

Please see Important Safety Information, and see full Prescribing Information, including BOXED WARNING.

Important Safety Information

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 65% (all grades) of the 570 patients treated with PADCEV in combination with intravenous pembrolizumab for the treatment of MIBC in clinical trials. The majority of the skin reactions that occurred with combination therapy included rash and maculo-papular rash. Grade 3-4 skin reactions occurred in 13% of patients (Grade 3: 12%, Grade 4: 1.1%), including maculo-papular rash, rash, SJS, dermatitis, exfoliative generalized dermatitis, toxic skin eruption, acute generalized exanthematous pustulosis, bullous dermatitis, erythema, macular rash, and pruritic rash. A fatal reaction of TEN occurred in one patient (0.2%). The median time to onset of severe skin reactions was 0.6 months (range: 0.1 to 24 months). Skin reactions led to discontinuation of PADCEV in 8% of patients. Of the patients who experienced a skin reaction and had data regarding resolution (n=367), 87% had complete resolution and 13% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 31% (15/49) had Grade ≥2 skin reactions.

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.

Hyperglycemia and diabetic ketoacidosis (DKA), including fatal events, occurred in patients with and without preexisting diabetes mellitus, treated with PADCEV. Patients with baseline hemoglobin A1C ≥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 by 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 intravenous pembrolizumab for the treatment of MIBC, 7% of the 570 patients treated with combination therapy had pneumonitis/ILD of any grade and 1.8% had Grade 3-4. The median time to onset of any grade pneumonitis/ILD was 3.2 months (range: 0.7 to 13 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 intravenous pembrolizumab for the treatment of MIBC, 42% of the 570 patients treated with combination therapy had PN of any grade, 14% had Grade 2 neuropathy, and 3% had Grade 3 neuropathy. The median time to onset of Grade ≥2 PN was 4.9 months (range: 0.2 to 23 months). Of the patients who experienced neuropathy and had data regarding resolution (n=239), 41% had complete resolution, and 59% of patients had residual neuropathy at last evaluation. Of the patients with residual neuropathy at last evaluation, 30% (42/142) had Grade ≥2 neuropathy.

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 ≥3 PN.

Please see Important Safety Information, and see full Prescribing Information, including BOXED WARNING.

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

Important Safety Information (cont'd)

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.

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 (≥20%): decreased hemoglobin, increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), rash, increased creatinine, decreased lymphocytes, fatigue, pruritus, decreased sodium, PN, increased potassium, diarrhea, alopecia, dysgeusia, decreased appetite, nausea, constipation, urinary tract infection (UTI), dry eye, increased glucose, decreased weight, decreased potassium, hyperglycemia, decreased phosphate, and decreased neutrophils.

EV-304 Study: Patients with cisplatin-eligible MIBC (PADCEV in combination with intravenous pembrolizumab)

- **Neoadjuvant phase:** Of a total of 403 patients, **serious adverse reactions** occurred in 27% of patients receiving PADCEV in combination with intravenous pembrolizumab; the most common (≥1.5%) were rash (3.2%), pneumonitis/ILD (2.2%), and diarrhea (1.7%). **Fatal adverse reactions** occurred in 1.7% of patients, including multiple organ dysfunction syndrome (0.5%) and COVID-19 pneumonia, cardiac arrest, pneumonia, septic shock, and urosepsis (0.2% each). Additional fatal adverse reactions were reported in 2 patients in the post-surgery phase before adjuvant treatment started, including pneumonia and sepsis (1 patient each). **Adverse reactions leading to discontinuation** of PADCEV in the neoadjuvant phase occurred in 21% of patients; the most common (≥1%) were PN (5%) and rash (3.5%). **Adverse reactions leading to dose interruption** of PADCEV in the neoadjuvant phase occurred in 35% of patients; the most common (≥2%) were rash (10%), increased ALT (4%), neutropenia (3.7%), hyperglycemia (3%). **Adverse reactions leading to dose reduction** of PADCEV in the neoadjuvant phase occurred in 15% of patients; the most common (≥1%) were rash (9%) and pruritus (2%). Of the 403 patients in the PADCEV in combination with intravenous pembrolizumab arm who received neoadjuvant treatment, thirteen (3.2%) patients did not receive surgery due to adverse reactions. The **adverse reactions that led to cancellation of surgery** were multiple organ dysfunction syndrome (0.5%) and adenocarcinoma of colon, COVID-19 pneumonia, cardiac arrest, chronic obstructive pulmonary disease, coronary artery disease, glomerulonephritis, immune-mediated lung disease, myocarditis, pneumonia, pneumonitis, and urosepsis (0.2% each). Of the 351 patients who received neoadjuvant treatment with PADCEV in combination with intravenous pembrolizumab and underwent radical cystectomy (RC), 26 (7%) patients experienced delay of surgery due to adverse reactions.
- **Adjuvant phase:** Of the 351 patients who underwent surgery, 225 patients received adjuvant treatment with PADCEV with or without intravenous pembrolizumab. Of the 126 patients who did not receive adjuvant PADCEV, discontinuation of PADCEV prior to the adjuvant phase was due to an adverse event in 65 patients. **Serious adverse reactions** occurred in 36% of patients receiving PADCEV; the most common (≥1.5%) included UTI (8%), sepsis (2.2%), and diarrhea, hyperglycemia, pneumonitis/ILD, and urosepsis (1.8% each). **Fatal adverse reactions** occurred in 3.1% of patients and included cardiac arrest, death, duodenal ulcer perforation, acute pancreatitis, renal failure, small cell lung cancer, and toxic shock syndrome (0.4% each). **Adverse reactions leading to discontinuation** of PADCEV in the adjuvant phase occurred in 16% of patients; the most common (≥1%) were rash (3.6%), PN (1.8%), and UTI (1.3%). **Adverse reactions leading to dose**

Please see Important Safety Information, and see full Prescribing Information, including BOXED WARNING.

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

Important Safety Information (cont'd)

interruption of PADCEV® in the adjuvant phase occurred in 34% of patients; the most common (≥2%) were diarrhea and UTI (5% each), rash (4%), and COVID-19 (2.7%). **Adverse reactions leading to dose reduction** of PADCEV in the adjuvant phase occurred in 5% of patients; the most common (>1%) included rash (1.3%).

EV-303 Study: Patients with cisplatin-ineligible MIBC (PADCEV in combination with intravenous pembrolizumab)

- **Neoadjuvant phase:** Of a total of 167 patients, **serious adverse reactions** occurred in 27% of patients receiving PADCEV in combination with intravenous pembrolizumab; the most frequent (≥2%) were UTI (3.6%) and hematuria (2.4%). **Fatal adverse reactions** occurred in 1.2% of patients including myasthenia gravis and TEN (0.6% each). Additional fatal adverse reactions were reported in 2.7% of patients in the post-surgery phase before adjuvant treatment started, including sepsis and intestinal obstruction (1.4% each). **Adverse reactions leading to discontinuation** of PADCEV occurred in 22% of patients; the most common (≥1%) were rash (4.8%), PN (2.4%), and diarrhea, dysgeusia, fatigue, pruritus, and TEN (1.2% each). **Adverse reactions leading to dose interruption** of PADCEV occurred in 29% of patients; the most common (≥2%) were rash (8%), neutropenia (3.6%), hyperglycemia (3%), and fatigue and PN (2.4% each). **Adverse reactions leading to dose reduction** of PADCEV occurred in 13% of patients; the most common (≥1%) were rash (4.8%), pruritus (1.8%), and PN, increased ALT, increased AST, decreased appetite, fatigue, neutropenia, and decreased weight (1.2% each). Seven (4.2%) patients did not receive surgery due to adverse reactions. The **most common adverse reactions that led to cancellation of surgery** were acute myocardial infarction, bile duct cancer, colon cancer, respiratory distress, UTI and deaths due to myasthenia gravis and TEN (0.6% each). Of the 146 patients who received neoadjuvant treatment with PADCEV in combination with intravenous pembrolizumab and underwent RC, six (4.1%) patients experienced delay of surgery due to adverse reactions.
- **Adjuvant phase:** Of the 146 patients who underwent surgery, 92 patients received adjuvant treatment with PADCEV with or without intravenous pembrolizumab. Of the 54 patients who did not receive adjuvant PADCEV, discontinuation of PADCEV prior to the adjuvant phase was due to an adverse event in 27 patients. **Serious adverse reactions** occurred in 43% of patients receiving PADCEV; the most frequent (≥2%) were UTI (8%), acute kidney injury, pyelonephritis, and urosepsis (4.3% each), and hypokalemia, intestinal obstruction, and sepsis (2.2% each). **Fatal adverse reactions** occurred in 8% of patients, including urosepsis, hemorrhage intracranial, death, myocardial infarction, multiple organ dysfunction syndrome, and pneumonia pseudomonal (1.1% each). **Adverse reactions leading to discontinuation** of PADCEV occurred in 28% of patients; the most common (≥2%) were PN (5%) and rash (4.3%). **Adverse reactions leading to dose interruption** of PADCEV occurred in 39% of patients; the most common (≥2%) were rash (7%), diarrhea and UTI (5% each), fatigue (4.3%), pruritus (3.3%), and PN and pyelonephritis (2.2% each). **Adverse reactions leading to dose reduction** of PADCEV occurred in 8% of patients; the most common (≥2%) was weight decreased (2.2%).

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.

Perioperative PADCEV® + pembrolizumab was studied in two open-label, randomized, active-controlled, multicenter phase 3 trials in MIBC[1-3]

Perioperative treatment refers to systemic therapy given both before RC + PLND (neoadjuvant) and after RC + PLND (adjuvant)[1]

PERIOPERATIVE REGIMEN IN EV-304[1,4]

Cisplatin-eligible MIBC (N=405)

Neoadjuvant treatment	RC + PLND*	Adjuvant treatment
PADCEV + pembrolizumab 4 cycles 4 cycles	Surgery was scheduled ~4 months after neoadjuvant treatment initiation	PADCEV + pembrolizumab 5 cycles 13 cycles

→ Follow-up

Treatment continued until completion of the treatment, disease progression, not undergoing or refusal of RC + PLND, disease recurrence in the adjuvant phase, or unacceptable toxicity.

Based on EV-304, an open-label, randomized, multicenter phase 3 trial in which patients with MIBC were randomized 1:1 to perioperative PADCEV + pembrolizumab (n=405) or neoadjuvant gemcitabine + cisplatin chemotherapy (n=403). Patients who had previously untreated MIBC with ≥50% urothelial carcinoma histology, were candidates for RC + PLND, and were eligible for cisplatin-based chemotherapy were included. Both study arms received RC + PLND. The primary endpoint was EFS by BICR, and key secondary endpoints were OS and pCR rate by BIPR. Neoadjuvant PADCEV was dosed at 1.25 mg/kg IV on days 1 and 8 in combination with pembrolizumab IV 200 mg on day 1 of a 21-day cycle for 4 cycles prior to surgery, followed by adjuvant PADCEV for up to 5 cycles and pembrolizumab for up to 13 cycles (21 days per cycle). In the comparator arm, patients received neoadjuvant gemcitabine 1000 mg/m^2 on days 1 and 8 and cisplatin 70 mg/m^2 on day 1 of each 21-day cycle for 4 cycles prior to surgery, followed by observation.[1,4†]

PERIOPERATIVE REGIMEN IN EV-303[1-3]

Cisplatin-ineligible MIBC (N=170)

Neoadjuvant treatment	RC + PLND*	Adjuvant treatment
PADCEV + pembrolizumab 3 cycles 3 cycles	Surgery was scheduled ~3 months after neoadjuvant treatment initiation	PADCEV + pembrolizumab 6 cycles 14 cycles

→ Follow-up

Treatment continued until completion of the treatment, disease progression, not undergoing or refusal of RC + PLND, disease recurrence in the adjuvant phase, or unacceptable toxicity.

Based on EV-303, an open-label, randomized, multicenter phase 3 trial in which patients with MIBC were randomized 1:1 to perioperative PADCEV + pembrolizumab (n=170) or RC + PLND alone (n=174). Patients who had previously untreated MIBC with ≥50% urothelial carcinoma histology, were candidates for RC + PLND, and were ineligible for or declined cisplatin-based chemotherapy were included. The primary endpoint was EFS by BICR, and key secondary endpoints were OS and pCR rate by BIPR. Neoadjuvant PADCEV was dosed at 1.25 mg/kg IV on days 1 and 8 in combination with pembrolizumab IV 200 mg on day 1 of a 21-day cycle for 3 cycles prior to surgery, followed by adjuvant PADCEV for up to 6 cycles and pembrolizumab for up to 14 cycles (21 days per cycle).[1-3†]

*Time frame around RC + PLND included pre- and post-surgery screening and follow-up.[3,4]

†Adjuvant nivolumab was permitted in the control arm for patients who were at high risk of recurrence after RC + PLND as defined by the approved product label, if locally available, and if the patient was deemed appropriate per investigator. In the EV-303 trial, adjuvant nivolumab was used in 17% of patients enrolled in the RC + PLND arm.[1,3,4]

BICR=blinded independent central review; **BIPR**=blinded independent pathology review; **EFS**=event-free survival; **IV**=intravenous; **OS**=overall survival; **pCR**=pathologic complete response; **RC + PLND**=radical cystectomy + pelvic lymph node dissection.

Please see Important Safety Information, and see full Prescribing Information, including BOXED WARNING.

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

Clinical trial results with perioperative PADCEV® + pembrolizumab

VS NEOADJUVANT GEM-CIS (EV-304)

Cisplatin-eligible MIBC

EFS* by BICR[1]—Superior event-free survival (EFS)

47% REDUCTION IN RISK OF AN EVENT vs **Neoadjuvant gem-cis**

(HR=0.53[†]; 95% CI: 0.41, 0.70; *P*<0.0001[‡])

Number of events: 87/405 (21%) with perioperative PADCEV + pembrolizumab vs 146/403 (36%) with neoadjuvant gem-cis

mEFS[§] NR (95% CI: NR, NR) vs 48.5 months (95% CI: 43.3, NR)

OS[1]—Superior overall survival (OS)

35% REDUCTION IN RISK OF DEATH vs **Neoadjuvant gem-cis**

(HR=0.65[†]; 95% CI: 0.48, 0.89; *P*=0.0029[‡])

Number of events: 69/405 (17%) with perioperative PADCEV + pembrolizumab vs 99/403 (25%) with neoadjuvant gem-cis

mOS[§] NR (95% CI: NR, NR) vs NR (95% CI: NR, NR)

pCR[‖] rate by BIPR[1,5]—Nearly 60% of patients in the PADCEV + pembrolizumab arm achieved pCR in both MIBC trials

55.8% (95% CI: 50.8, 60.7) **With PADCEV + pembrolizumab** (n=226/405)

***P*<0.0001**

vs neoadjuvant gem-cis (n=131/403): 32.5% (95% CI: 28.0, 37.3)

VS RC + PLND ALONE (EV-303)

Cisplatin-ineligible MIBC

EFS* by BICR[1]—Superior event-free survival (EFS)

60% REDUCTION IN RISK OF AN EVENT vs **RC + PLND alone**

(HR=0.40[†]; 95% CI: 0.28, 0.57; *P*<0.0001[‡])

Number of events: 48/170 (28%) with perioperative PADCEV + pembrolizumab vs 95/174 (55%) with RC + PLND alone

mEFS[§] (95% CI: 37.3, NR) vs 15.7 months (95% CI: 10.3, 20.5)

OS[1]—Superior overall survival (OS)

50% REDUCTION IN RISK OF DEATH vs **RC + PLND alone**

(HR=0.50[†]; 95% CI: 0.33, 0.74; *P*=0.0002[‡])

Number of events: 38/170 (22%) with perioperative PADCEV + pembrolizumab vs 68/174 (39%) with RC + PLND alone

mOS[§] NR (95% CI: NR, NR) vs 41.7 months (95% CI: 31.8, NR)

pCR[‖] rate by BIPR[1,2]—Nearly 60% of patients in the PADCEV + pembrolizumab arm achieved pCR in both MIBC trials

57.1% (95% CI: 49.3, 64.6) **With PADCEV + pembrolizumab** (n=97/170)

***P*<0.0001**

vs RC + PLND alone (n=15/174): 8.6% (95% CI: 4.9, 13.8)

Trial results are not comparable across studies.

*An event was defined as the first occurrence of any of the following: disease progression preventing curative RC + PLND; failure to undergo RC + PLND for participants with muscle-invasive residual disease; incomplete surgical resection; local or distant recurrence after RC + PLND; or death. Event-free survival (EFS) was defined as the time from randomization to the occurrence of an event.[1]

[†]Based on stratified Cox regression model.[1]

[‡]One-sided p-value based on stratified log-rank test.[1,2]

[§]Based on Kaplan-Meier estimates.[1]

[‖]pCR was defined as absence of viable tumor (pT0N0) in examined tissue from RC + PLND, as assessed by BIPR.[1,2,5]

CI=confidence interval; **gem-cis**=gemcitabine-cisplatin; **HR**=hazard ratio; **mEFS**=median event-free survival; **mOS**=median overall survival; **NR**=not reached.

Please see Important Safety Information, and see full Prescribing Information, including BOXED WARNING.

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

Perioperative PADCEV® + pembrolizumab: 9 planned cycles of PADCEV across neoadjuvant and adjuvant treatment

The perioperative treatment regimen: Dosing for MIBC 21-day treatment cycle[1]

	NEOADJUVANT		ADJUVANT
	DAY 1 › DAY 8 › DAY 15	RC + PLND	DAY 1 › DAY 8 › DAY 15
PADCEV ***1.25 mg/kg IV*** ***⚠ (up to a maximum dose of 125 mg) on days 1 and 8 of a 21-day cycle*** 30-minute infusion time for PADCEV	**CISPLATIN ELIGIBLE: 4 CYCLES** **CISPLATIN INELIGIBLE: 3 CYCLES** Treatment until completion of cycles, disease progression that precludes curative-intent RC + PLND, or unacceptable toxicity		**CISPLATIN ELIGIBLE: 5 CYCLES** **CISPLATIN INELIGIBLE: 6 CYCLES** Treatment until completion of the treatment, disease recurrence, or unacceptable toxicity
Pembrolizumab ***Based on IV (200 mg) administered on day 1 of every 21-day cycle, as studied in MIBC trials***	**CISPLATIN ELIGIBLE: 4 CYCLES** **CISPLATIN INELIGIBLE: 3 CYCLES** Treatment until completion of cycles, disease progression that precludes curative-intent RC + PLND, or unacceptable toxicity	RC + PLND	**CISPLATIN ELIGIBLE: 13 CYCLES** **CISPLATIN INELIGIBLE: 14 CYCLES** Treatment until completion of the treatment, disease recurrence, or unacceptable toxicity

PADCEV can be given with pembrolizumab IV or subcutaneous pembrolizumab + berahyaluronidase alfa-pmph.* For more information on recommended dosage of pembrolizumab or pembrolizumab + berahyaluronidase alfa-pmph, refer to the respective Prescribing Information.[1]

*Administer PADCEV prior to pembrolizumab or pembrolizumab + berahyaluronidase alfa-pmph if administering on the same day.[1]

ASPECTS OF PADCEV DOSING AND ADMINISTRATION

Premedication is not required[3†]

PADCEV: 30-minute infusion time[1]

†Premedication is not specified in the US Prescribing Information. In the EV-303 trial, patients who experienced an infusion-related reaction (IRR) may have been premedicated for subsequent infusions.[3]

Premedication for IRRs may have included pain medicine (eg, acetaminophen or equivalent), an antihistamine (eg, diphenhydramine hydrochloride), and a corticosteroid administered approximately 30 to 60 minutes prior to each PADCEV infusion.[3]

Please see Important Safety Information, and see full Prescribing Information, including BOXED WARNING.

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

PADCEV® dosage and administration[1]

Recommended starting dose calculation

The amounts shown in the dosing calculation below are based on the recommended dose of PADCEV (1.25 mg/kg [up to a maximum of 125 mg for patients ≥100 kg], administered as an IV infusion over 30 minutes) and do not include dose modifications. This calculation should not replace professional judgment or clinical experience.

When resuming PADCEV treatment after withholding due to an adverse reaction, consult the dose modifications table to determine the appropriate dose level.

$$\left(\frac{\text{Patient weight (lbs)}}{2.2}\right) \times 1.25 = \text{DOSE (mg)}$$

Access the **PADCEV dosing calculator** for help determining your patient's recommended dose

Recommended starting dose of PADCEV and dose reduction schedule

During the course of treatment, certain adverse reactions may require dose modifications.

Starting dose	1st dose **reduction**	2nd dose **reduction**	3rd dose **reduction**
DOSE LEVEL: **1.25 mg/kg up to 125 mg**	DOSE LEVEL: **1 mg/kg up to 100 mg**	DOSE LEVEL: **0.75 mg/kg up to 75 mg**	DOSE LEVEL: **0.5 mg/kg up to 50 mg**

Please see Important Safety Information, and see full Prescribing Information, including BOXED WARNING.

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

PADCEV® dose modifications[1]

ADVERSE REACTION	SEVERITY*	DOSE MODIFICATION*
SKIN REACTIONS	For persistent or recurrent Grade 2 skin reactions	■ **Consider withholding** until Grade ≤1 ▫ Then **resume** treatment at the same dose level or dose reduce by one dose level
	Grade 3 skin reactions	■ **Withhold** until Grade ≤1 ▫ Then **resume** treatment at the same dose level or dose reduce by one 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**
HYPERGLYCEMIA	Blood glucose >250 mg/dL	■ **Withhold** until elevated blood glucose has improved to ≤250 mg/dL ▫ Then **resume** treatment at the same dose level
PNEUMONITIS/ INTERSTITIAL LUNG DISEASE (ILD)	Grade 2	■ **Withhold** until Grade ≤1 ▫ Then **resume** treatment at the same dose level or consider dose reduction by one dose level
	Grade ≥3	■ **Permanently discontinue**
PERIPHERAL NEUROPATHY	Grade 2	■ **Withhold** until Grade ≤1 ▫ Then **resume** treatment at the same dose level (if first occurrence) ■ For a recurrence, **withhold** until Grade ≤1 ▫ Then **resume** treatment reduced by one dose level
	Grade ≥3	■ **Permanently discontinue**
OCULAR DISORDERS	N/A	■ **Consider dose interruption** or dose reduction of PADCEV for symptomatic ocular disorders
INFUSION SITE EXTRAVASATION	N/A	■ **Stop the infusion** and monitor for adverse reactions
OTHER NONHEMATOLOGIC TOXICITY	Grade 3	■ **Withhold** until Grade ≤1 ▫ Then **resume** treatment at the same dose level or consider dose reduction by one dose level
	Grade 4	■ **Permanently discontinue**
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 one dose level
	Grade 4	■ **Withhold** until Grade ≤1 ▫ Then reduce dose by one dose level or **discontinue treatment**

■ WITHHOLD ■ RESUME ■ DISCONTINUE

It is important to proactively monitor, identify, and help manage adverse reactions that may arise during treatment

*Grade 1 is mild; Grade 2 is moderate; Grade 3 is severe; Grade 4 is life-threatening.
SJS=Stevens-Johnson syndrome; **TEN**=toxic epidermal necrolysis.

Please see Important Safety Information, and see full Prescribing Information, including BOXED WARNING.

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

If you have any questions or would like more information about PADCEV® dosing and administration:

Call 1-888-4PADCEV (1-888-472-3238) or visit PADCEVhcp.com

Contact your PADCEV representative for additional resources, and visit PADCEVhcp.com for more helpful tools

Please see Important Safety Information and see full Prescribing Information, including BOXED WARNING.

References: 1. PADCEV. Package insert. Northbrook, IL: Astellas Pharma US, Inc; 2026. **2.** Vulsteke C, Adra N, Danchaivijitr P, et al; for the KEYNOTE-905/EV-303 Investigators. Perioperative enfortumab vedotin and pembrolizumab in bladder cancer [published online ahead of print February 18, 2026]. *N Engl J Med*. 2026. Accessed February 20, 2026. https://www.nejm.org/doi/pdf/10.1056/NEJMoa2511674. **3.** Protocol for: Vulsteke C, Adra N, Danchaivijitr P, et al; for the KEYNOTE-905/EV-303 Investigators. Perioperative enfortumab vedotin and pembrolizumab in bladder cancer [published online ahead of print February 18, 2026]. *N Engl J Med*. 2026. Accessed February 20, 2026. https://www.nejm.org/doi/pdf/10.1056/NEJMoa2511674. **4.** Pfizer Inc. and Astellas. PADCEV. Data on File. **5.** Galsky MD, Pérez-Valderrama B, Maruzzo M, et al. Neoadjuvant and adjuvant enfortumab vedotin plus pembrolizumab for participants with muscle-invasive bladder cancer who are eligible for cisplatin: randomized, open-label, phase 3 KEYNOTE-B15 study. Presented at: American Society of Clinical Oncology Genitourinary Cancers Symposium; February 26-28, 2026; San Francisco, CA.

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

© 2026 Astellas Pharma Inc. or its affiliates and Pfizer Inc. All rights reserved. MAT-US-PAD-2026-00088 07/26
All trademarks are the property of their respective owners.