PADCEV® DOSING AND ADMINISTRATION

POCKET GUIDE

For cisplatin-ineligible muscle-invasive bladder cancer (MIBC)[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) who are ineligible for cisplatin-containing chemotherapy.

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

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

Important Safety Information

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) who are ineligible for cisplatin-containing chemotherapy.

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 61% (all grades) of the 167 patients treated with PADCEV in combination with intravenous pembrolizumab for the treatment of MIBC in clinical trials. The majority of skin reactions that occurred included rash and maculo-papular rash. Grade 3-4 skin reactions occurred in 10% of patients (Grade 3: 9%, Grade 4: 1.2%), including rash, maculo-papular rash, toxic skin eruption, dermatitis exfoliative generalized, erythema, exfoliative rash, skin toxicity, toxic epidermal necrolysis, and toxic erythema of chemotherapy. A fatal reaction of toxic epidermal necrolysis occurred in one patient (0.6%). The median time to onset of severe skin reactions was 0.6 months (range: 0.2 to 8.8 months). Skin reactions led to discontinuation of PADCEV in 10% of patients. Of the patients who experienced a skin reaction and had data regarding resolution (n=102), 83% had complete resolution and 17% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 29% (5/17) 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 pre-existing 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 diabetic ketoacidosis 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, 4.2% of the 167 patients had pneumonitis/ILD of any grade. All events were Grade 1-2. The median time to onset of any grade pneumonitis/ILD was 2.5 months (range: 1.9 to 9.7 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, 39% of the 167 patients had PN of any grade, 12% had Grade 2 neuropathy, and 3% had Grade 3 neuropathy. The median time to onset of Grade ≥2 PN was 4.7 months (range: 0.2 to 11 months). Of the patients who experienced neuropathy and had data regarding resolution (n=65), 32% had complete resolution, and 68% of patients had residual neuropathy at last evaluation. Of the patients with residual neuropathy at last evaluation, 27% (12/44) 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.

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

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

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

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%) serious adverse reactions were urinary tract infection (3.6%) and hematuria (2.4%). **Fatal adverse reactions** occurred in 1.2% of patients including myasthenia gravis and toxic epidermal necrolysis (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 adverse reactions (≥1%) leading to discontinuation of PADCEV were rash (4.8%), peripheral neuropathy (2.4%), and diarrhea, dysgeusia, fatigue, pruritus, and toxic epidermal necrolysis (1.2% each). **Adverse reactions leading to dose interruption** of PADCEV occurred in 29% of patients. The most common adverse reactions (≥2%) leading to dose interruption of PADCEV were rash (8%), neutropenia (3.6%), and hyperglycemia (3%), and fatigue and peripheral neuropathy (2.4% each). **Adverse reactions leading to dose reduction** of PADCEV occurred in 13% of patients. The most common adverse reactions (≥1%) leading to dose reduction of PADCEV were rash (4.8%), pruritus (1.8%), and peripheral neuropathy, increased alanine aminotransferase, increased aspartate aminotransferase, decreased appetite, fatigue, neutropenia, and decreased weight (1.2% each). Seven (4.2%) patients did not receive surgery due to adverse reactions. The **adverse reactions that led to cancellation of surgery** were acute myocardial infarction, bile duct cancer, colon cancer, respiratory distress, urinary tract infection and deaths due to myasthenia gravis and toxic epidermal necrolysis (0.6% each). Of the 146 patients who received neoadjuvant treatment with PADCEV in combination with intravenous pembrolizumab and underwent RC, 6 (4.1%) patients experienced delay of surgery due to adverse reactions.
- **Adjuvant phase:** Of the 149 patients who underwent surgery, 100 patients received adjuvant treatment with PADCEV in combination with intravenous pembrolizumab. Of the 49 patients who did not receive adjuvant treatment, discontinuation of treatment with PADCEV in combination with intravenous pembrolizumab prior to the adjuvant phase was due to an adverse event in 21 patients. **Serious adverse reactions** occurred in 43% of patients receiving PADCEV in combination with pembrolizumab. The most frequent (≥2%) serious adverse reactions were urinary tract infection (8%), acute kidney injury and pyelonephritis (5% each), urosepsis (4%), and hypokalemia, intestinal obstruction, and sepsis (2% each). **Fatal adverse reactions** occurred in 7% of patients, including urosepsis, hemorrhage intracranial, death, myocardial infarction, multiple organ dysfunction syndrome, and pneumonia pseudomonal (1% each). **Adverse reactions leading to discontinuation** of PADCEV occurred in 26% of patients. The most common adverse reactions (≥2%) leading to discontinuation of PADCEV were peripheral neuropathy (5%) and rash (4%). **Adverse reactions leading to dose interruption** of PADCEV occurred in 36% of patients. The most common adverse reactions (≥2%) leading to dose interruption of PADCEV were rash (6%), diarrhea and urinary tract infection (5% each), fatigue (4%), pruritus (3%), and peripheral neuropathy and pyelonephritis (2% each). **Adverse reactions leading to dose reduction** of PADCEV occurred in 7% of patients. The most common adverse reactions (≥2%) leading to dose reduction of PADCEV was weight decreased (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.

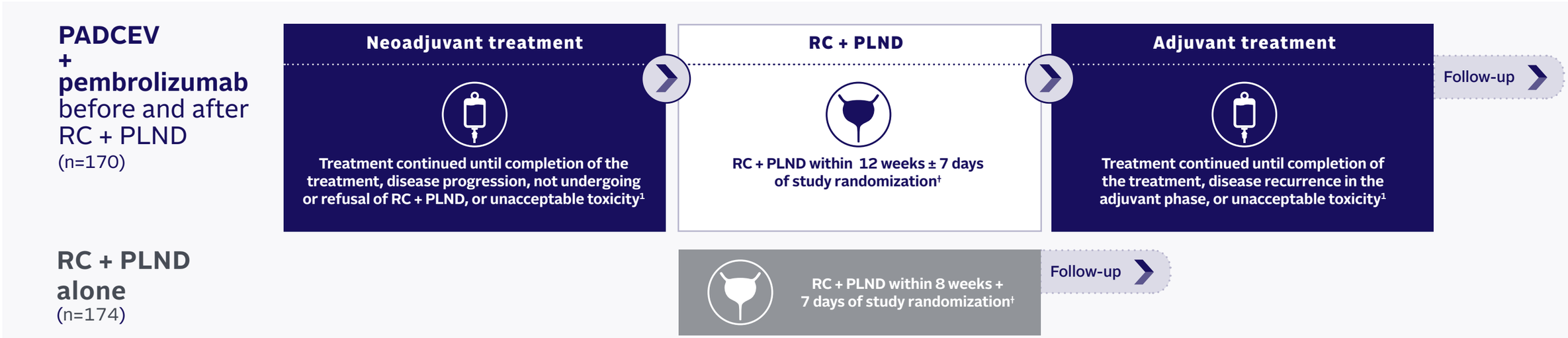
Please see Important Safety Information and full Prescribing Information, including BOXED WARNING.

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

Clinical trial overview and efficacy results

EV-303 trial: Perioperative PADCEV® + pembrolizumab in cisplatin-ineligible patients with MIBC[1-3]*

Perioperative treatment refers to systemic therapy given both before RC + PLND (neoadjuvant) and after RC + PLND (adjuvant)[2]



*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, were candidates for RC + PLND, and were ineligible for or declined cisplatin-based chemotherapy were included. The primary endpoint was EFS per BICR, and key secondary endpoints were OS and pCR rate by BIPR.[1,3]

†RC + PLND can occur outside this time frame if delay due to an AE.[3]

Perioperative PADCEV + pembrolizumab demonstrated a 60% reduction in risk of an event vs RC + PLND alone[1]

Primary endpoint

EFS‡ by BICR[1]

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

(HR=0.40§; 95% CI: 0.28, 0.57; *P*<0.0001‖)

mEFS¶ NR (95% CI: 37.3, NR) with perioperative PADCEV + pembrolizumab vs 15.7 months (95% CI: 10.3, 20.5) with RC + PLND alone

Key secondary endpoints

OS[1]

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

(HR=0.50§; 95% CI: 0.33, 0.74; *P*=0.0002‖)

mOS¶ NR (95% CI: NR, NR) with perioperative PADCEV + pembrolizumab vs 41.7 months (95% CI: 31.8, NR) with RC + PLND alone

pCR# rate by BIPR[1,2]

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

P<0.0001

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

Event=failure to undergo RC + PLND due to progression or residual disease, incomplete surgical resection or disease recurrence after, or death.[1,3]

AE=adverse event; BICR=blinded independent central review; BIPR=blinded independent pathology review; CI=confidence interval; EFS=event-free survival; HR=hazard ratio; mEFS=median event-free survival; mOS=median overall survival; NR=not reached; OS=overall survival; pCR=pathological complete response; PLND=pelvic lymph node dissection; RC=radical cystectomy.

‡EFS is defined as time from randomization to the first of: 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.[1,3]

§Based on stratified Cox regression model.[1]

‖Based on stratified log-rank test.[1]

¶Based on Kaplan-Meier estimates.[1]

#pCR was defined as absence of viable tumor (pTONO) in examined tissue from RC + PLND, as assessed by BIPR.[1,3]

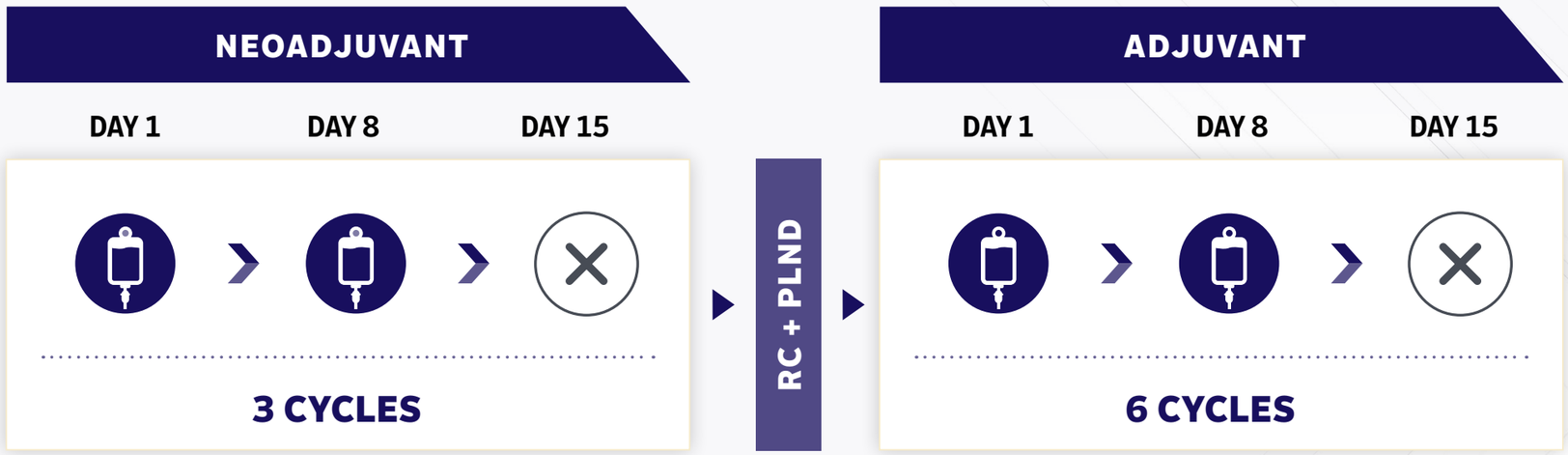
Please see Important Safety Information and full Prescribing Information, including BOXED WARNING.

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

PADCEV® + pembrolizumab: Dosing for cisplatin-ineligible MIBC 21-day treatment cycle[1]

The perioperative treatment regimen includes 9 total cycles of PADCEV. PADCEV can be given with pembrolizumab IV or subcutaneous pembrolizumab + berahyaluronidase alfa-pmph*

PADCEV
1.25 mg/kg IV
⚠ up to a maximum dose of 125 mg
30-minute infusion time for PADCEV



Treatment until completion of cycles, disease progression that precludes RC + PLND, or unacceptable toxicity

Treatment until completion of the treatment, disease recurrence, or unacceptable toxicity

For the recommended dosage of pembrolizumab or pembrolizumab + berahyaluronidase alfa-pmph, refer to the respective Prescribing Information.

*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. 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 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.

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

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 **level**	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**

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

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

PADCEV® dose modifications due to adverse reactions[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**

ADVERSE REACTION	SEVERITY*	DOSE MODIFICATION*
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 manage adverse reactions that may arise during treatment.

SJS=Stevens-Johnson syndrome; TEN=toxic epidermal necrolysis.

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

Please see Important Safety Information and 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

References: 1. PADCEV. Package insert. Northbrook, IL: Astellas Pharma US, Inc; 2025. **2.** Vulsteke C, Kaimakliotis HZ, Danchaivijitr P, et al. Perioperative enfortumab vedotin plus pembrolizumab in participants with muscle-invasive bladder cancer who are cisplatin-ineligible: phase 3 KEYNOTE-905 study. Previously presented at: European Society of Medical Oncology (ESMO); Final Publication Number LBA2; October 17-21, 2025; Berlin, Germany. Reused with permission. **3.** Pfizer Inc. and Astellas. PADCEV. Data on File.

astellas

Pfizer Oncology

© 2025 Astellas Pharma Inc. or its affiliates and Pfizer Inc. All rights reserved. MAT-US-PAD-2025-00708 11/25
All trademarks are the property of their respective owners.

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