Locally advanced or mUC

PADCEV® DOSING AND ADMINISTRATION

POCKET GUIDE

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.

mUC=metastatic urothelial cancer.

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, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC).

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

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 intravenous pembrolizumab for the treatment of locally advanced or mUC in clinical trials. The majority of skin reactions that occurred 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. Of the patients who experienced a skin reaction and had data regarding resolution (n=391), 59% had complete resolution and 41% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 27% (43/159) 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 locally advanced or mUC, 10% of the 564 patients 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 median time to onset of any grade pneumonitis/ILD was 4 months (range: 0.3 to 26 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.

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Important Safety Information (cont'd)

Peripheral neuropathy (PN) When PADCEV® was given in combination with intravenous pembrolizumab for the treatment of locally advanced or mUC, 67% of the 564 patients had PN of any grade, 36% had Grade 2 neuropathy, and 7% had Grade 3 neuropathy. The median time to onset of Grade ≥2 PN was 6 months (range: 0.3 to 25 months). Of the patients who experienced neuropathy and had data regarding resolution (n=373), 13% had complete resolution, and 87% of patients had residual neuropathy at last evaluation. Of the patients with residual neuropathy at last evaluation, 45% (146/326) 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.

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%):

- **PADCEV in combination with intravenous pembrolizumab for the treatment of locally advanced or mUC:** increased aspartate aminotransferase (AST), increased creatinine, rash, increased glucose, peripheral neuropathy, 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.

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Important Safety Information (cont'd)

EV-302 Study: 440 patients with previously untreated locally advanced or mUC (PADCEV® in combination with intravenous pembrolizumab)

Serious adverse reactions occurred in 50% of patients treated with PADCEV in combination with intravenous pembrolizumab. The most common serious adverse reactions (≥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 intravenous 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 (≥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 (≥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 (≥2%) leading to dose reduction** of PADCEV were rash (16%), PN (13%) and fatigue (2.7%).

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.

PADCEV + pembrolizumab nearly doubled mOS vs chemotherapy

EV-302 trial: PADCEV in combination with pembrolizumab

PADCEV + pembrolizumab nearly doubled mOS vs platinum-based chemotherapy in previously untreated patients with locally advanced or mUC[1]

mOS

PADCEV + pembrolizumab (n=442)

31.5 months
(95% CI: 25.4, NE)

Platinum-based chemotherapy (n=444)

16.1 months
(95% CI: 13.9, 18.3)

(HR=0.47; 95% CI: 0.38, 0.58*; *P*<0.0001)†

EV-302 is an open-label, randomized, multicenter phase 3 trial of previously untreated locally advanced or mUC patients randomized 1:1 to PADCEV + pembrolizumab (n=442) vs platinum-based chemotherapy (gemcitabine with cisplatin or carboplatin; n=444). Dual primary endpoints were OS and PFS by BICR per RECIST v1.1. 12.5 months mPFS (95% CI: 10.4, 16.6) with PADCEV + pembrolizumab vs 6.3 months mPFS (95% CI: 6.2, 6.5) with chemotherapy (HR=0.45; 95% CI: 0.38, 0.54*; *P*<0.0001).† Additional endpoints included ORR (objective response rate) by BICR per RECIST v1.1; 68% ORR (95% CI: 63.1, 72.1) with PADCEV + pembrolizumab (n=437)‡ vs 44% ORR (95% CI: 39.7, 49.2) with chemotherapy (n=441)‡ (*P*<0.0001).§ 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, with treatment continuing until disease progression or unacceptable toxicity.[1]

*Based on a stratified Cox proportional hazards model.[1]

†Based on stratified log-rank test. Two-sided *P* value.[1]

‡Includes only patients with measurable disease at baseline.[1]

§Two-sided *P* value. Cochran-Mantel-Haenszel test (CMH) controlling for stratification factors.[1]

BICR=blinded independent central review; **CI**=confidence interval; **HR**=hazard ratio; **IV**=intravenous; **mOS**=median overall survival; **mPFS**=median progression-free survival; **NE**=not estimated; **OS**=overall survival; **PFS**=progression-free survival; **RECIST**=Response Evaluation Criteria in Solid Tumors.

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Recommended dosage and infusion schedule

PADCEV® + pembrolizumab combination dosing[1]

When given in combination, the recommended dose of PADCEV is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) administered as an intravenous infusion (IV).

Dosing for the locally advanced or mUC 21-day treatment cycle[1,2]

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

DAY 1 › DAY 8 › DAY 15 ✕ ▶ **Until disease progression or unacceptable toxicity**

Pembrolizumab
Based on IV (200 mg), as studied in the 1L locally advanced or mUC trial

Administered on day 1 of every 21-day cycle ▶ **Until disease progression 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.

ASPECTS OF PADCEV DOSING AND ADMINISTRATION

Premedication is not required[3‡]

PADCEV: 30-minute infusion time[1]

*In the absence of disease progression or unacceptable toxicity, pembrolizumab was continued for up to 2 years.[1]

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

‡Premedication is not specified in the US Prescribing Information. In the EV-302 trial, patients who experienced an infusion-related reaction may have been premedicated for subsequent infusions. Premedication 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 infusion or according to institutional standards.[3]

1L=first-line.

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PADCEV® dosage and administration

Recommended starting dose calculation[1]

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]) 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 dose reduction schedule[1]

During the course of treatment, certain adverse reactions may require dose modifications.[1]

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**

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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**

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 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.

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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

Access the complete
PADCEV Dosing and Administration Guide

View the
PADCEV Adverse Reactions Information Guide

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

References: 1. PADCEV. Package insert. Northbrook, IL: Astellas Pharma US, Inc; 2025. **2.** Keytruda. Package insert. Rahway, NJ: Merck Sharp & Dohme LLC; 2026. **3.** Protocol for: Powles T, Valderrama BP, Gupta S, et al; for the EV-302 Trial Investigators. Enfortumab vedotin and pembrolizumab in untreated advanced urothelial cancer. *N Engl J Med*. 2024;390(10):875-888.

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