**Locally advanced or mUC**

# CARE TEAM GUIDE TO PADCEV ADVERSE REACTIONS

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.

**1L**=first-line; **mUC**=metastatic urothelial cancer.

**NCCN CATEGORIES OF EVIDENCE AND CONSENSUS[1]**
**Category 1:** Based upon high-level evidence (≥1 randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.

**NCCN CATEGORIES OF PREFERENCE[1]**
**Preferred:** Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.

## 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.**

## INDICATIONS

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).

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.

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

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

## 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.

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. Of the patients who experienced a skin reaction and had data regarding resolution (n=328), 58% had complete resolution and 42% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 39% (53/137) 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 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 2 patients (0.4%). 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 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.

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 ≥2 PN was 4.9 months (range: 0.1 to 20 months). Neuropathy led to treatment discontinuation in 6% of patients. Of the patients who experienced neuropathy who had data regarding resolution (n=296), 11% had complete resolution, and 89% had residual neuropathy at the time of their last evaluation. Of the patients with residual neuropathy at last evaluation, 50% (132/262) had Grade ≥2 neuropathy.

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

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

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, 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 (UTI), and decreased platelets.
- **PADCEV as a single agent:** 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, and dry skin.

**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 (≥2%) were rash (6%), acute kidney injury (5%), pneumonitis/ILD (4.5%), UTI (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 (≥2%) 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 (≥2%) were rash (16%), PN (13%), and fatigue (2.7%).

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

**Serious adverse reactions** occurred in 47% of patients treated with PADCEV; the most common (≥2%) were UTI, 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 (≥2%) were PN (5%) and rash (4%). **Adverse reactions leading to dose interruption** occurred in 61% of patients; the most common (≥4%) were PN (23%), rash (11%), and fatigue (9%). **Adverse reactions leading to dose reduction** occurred in 34% of patients; the most common (≥2%) were PN (10%), rash (8%), decreased appetite (3%), and fatigue (3%).

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

**Serious adverse reactions** occurred in 39% of patients treated with PADCEV; the most common (≥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**

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

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

**to discontinuation** occurred in 20% of patients; the most common (≥2%) was PN (7%). **Adverse reactions leading to dose interruption** occurred in 60% of patients; the most common (≥3%) were PN (19%), rash (9%), fatigue (8%), diarrhea (5%), increased AST (3%), and hyperglycemia (3%). **Adverse reactions leading to dose reduction** occurred in 49% of patients; the most common (≥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.

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

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

# What you will find inside this guide

Whether your patient is starting or continuing treatment with PADCEV®, regular monitoring for adverse reactions (ARs) is important while a patient is on this therapy.

This guide provides key information about PADCEV treatment, both in combination with pembrolizumab as a first-line (1L) therapy and as monotherapy in second-line (2L+) locally advanced or mUC populations.

**Inside this guide you will find:**

- Clinical trial efficacy results
- Dosing and infusion schedule
- Dose modification, interruption, and discontinuation information
- Clinical trial AR data and safety information
- Guidance on identifying and helping manage ARs
- Abbreviations (listed on the last page)

The AR information provided within this guide is based on the data available from PADCEV trials and other clinical sources. You will be able to differentiate between data from the 1L combination trials and 2L+ monotherapy trials using the following visual cues:

**1L** Combination data will be marked with a yellow icon and label, representing patients treated in 1L with PADCEV + pembrolizumab

**2L+** Monotherapy data will be marked with a blue icon and label, representing patients treated in 2L+ with PADCEV as monotherapy

## Support patients through awareness and communication

By increasing awareness of potential ARs and encouraging patients to share new or worsening symptoms right away, you can help promote the safe and effective use of PADCEV.[2]

### Increase awareness of ARs associated with treatment

Encourage patients to familiarize themselves with potential ARs observed in PADCEV clinical trials and emphasize the importance of immediately notifying their care team about any symptoms as soon as they occur.[2]

### Collaborate with the patient and caregiver

Ensure your patients understand the importance of promptly reporting symptoms as they arise. Encouraging open and regular communication about their condition and treatment can help you provide appropriate assistance as soon as possible.[2]

### Educate on the role of dose modifications

Help your patients understand the role of dose modifications in addressing ARs, and let them know that dose modifications were implemented as part of AR management in PADCEV clinical trials.[2]

Visit **PADCEVhcp.com** for more information about how PADCEV was shown to help patients with locally advanced or mUC.

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

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

# Clinical trial efficacy results

## 1L 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 metastatic UC[2]

**mOS**

| PADCEV + pembrolizumab (n=442) | Platinum-based chemotherapy (n=444) |
|---|---|
| **31.5 months** (95% CI: 25.4, NE) | **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, phase 3, randomized trial of previously untreated locally advanced or metastatic UC 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).[2,3§]

*Based on a stratified Cox proportional hazards model.[2]

†Based on stratified log-rank test. Two-sided *P* value.[2]

‡Includes only patients with measurable disease at baseline.[2]

§Two-sided *P* value. Cochran-Mantel-Haenszel test (CMH) controlling for stratification factors.[2]

## 2L+ EV-301 trial: PADCEV monotherapy

PADCEV significantly improved mOS‖ vs chemotherapy in patients with locally advanced or metastatic UC who were previously treated with a platinum-containing chemotherapy and a PD-(L)1 inhibitor[2]

**mOS**

| PADCEV (n=301) | Chemotherapy (n=307) |
|---|---|
| **12.9 months** (95% CI: 10.6, 15.2) | **9.0 months** (95% CI: 8.1, 10.7) |

(HR=0.70; 95% CI: 0.56, 0.89; *P*=0.0014)

The EV-301 trial evaluated PADCEV vs investigator's choice chemotherapy in an open-label, randomized, multicenter, phase 3 trial of 608 patients with locally advanced or metastatic UC who had previously received platinum-containing chemotherapy and a PD-(L)1 inhibitor. The major efficacy outcome measures were OS, PFS, and ORR (overall response rate) assessed by investigator using RECIST v1.1. 5.6 months mPFS (95% CI: 5.3, 5.8) with PADCEV vs 3.7 months mPFS (95% CI: 3.5, 3.9) with chemotherapy (HR=0.62; 95% CI: 0.51, 0.75; *P*<0.0001).‖¶ 41% ORR (n=117/288, 95% CI: 34.9, 46.5) with PADCEV vs 18% ORR (n=53/296, 95% CI: 13.7, 22.8) with chemotherapy (*P*<0.0001).[2,4,5#**]

‖Based on log-rank test. Stratification factors were ECOG PS, region, and liver metastasis.[2]

¶PFS is defined as the time from the date of randomization until the date of radiological disease progression (per RECIST v1.1), or until death due to any cause.[6]

#Based on Cochran-Mantel-Haenszel test. Stratification factors were ECOG PS, region and liver metastasis.[2]

**ORR consisted of confirmed CR and PR per RECIST v1.1 as evaluated by investigator. CR was defined as the disappearance of all target and nontarget lesions. PR was defined as a ≥30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters.[2,4,7]

### SELECT SAFETY INFORMATION

**BOXED WARNING: SERIOUS SKIN REACTIONS.** PADCEV can cause severe and fatal cutaneous adverse reactions, including SJS and TEN. PADCEV has additional **WARNINGS AND PRECAUTIONS** for hyperglycemia, pneumonitis/interstitial lung disease (ILD), peripheral neuropathy, ocular disorders, infusion site extravasation, and embryo-fetal toxicity.

**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

# Recommended dosage and infusion schedule

## 1L PADCEV® + pembrolizumab combination dosing 21-day treatment cycle[2,8]

**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.**

*In the absence of disease progression or unacceptable toxicity, pembrolizumab was continued for up to 2 years.[2]
†Administer PADCEV prior to pembrolizumab or pembrolizumab + berahyaluronidase alfa-pmph if administering on the same day.[2]

## 2L+ PADCEV monotherapy dosing 28-day treatment cycle[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 › DAY 22 ▶ Until disease progression or unacceptable toxicity

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

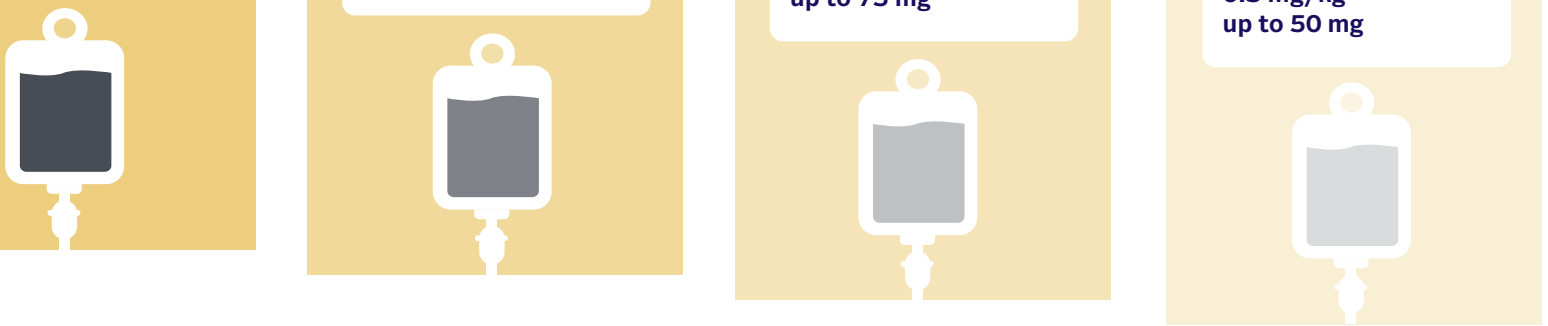
Please see Important Safety Information, and see full Prescribing Information, including BOXED WARNING.

# Modifying the dose of PADCEV®

Dose modifications may be implemented to help address select ARs.[2]

## RECOMMENDED STARTING DOSE OF PADCEV AND DOSE REDUCTION SCHEDULE[2]

| 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** |



Refer to the PADCEV Prescribing Information for the recommended dosing schedule of PADCEV as a single agent or in combination with pembrolizumab. For the recommended dosage of pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph, refer to the respective Prescribing Information.

Let your patients know that dose modifications were common in clinical trials with PADCEV. Encourage patients to promptly communicate any ARs to their care team.[2]

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

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

# Incidence rates and median times to onset for select warnings and precautions for PADCEV® when given in combination with pembrolizumab

## Select warnings and precautions

**These data are not generalizable and cannot be used to predict AR outcomes. The AR information for PADCEV in combination with pembrolizumab describes ARs observed with exposure to PADCEV at 1.25 mg/kg in combination with pembrolizumab in 564 patients in the EV-302 and EV-103 clinical trials.[2]**

ARs associated with PADCEV may occur shortly after the initiation of treatment, which is why it is important to be attentive from the beginning.[2]

Evaluate your patients for ARs at each visit, as they may occur at any time during treatment with PADCEV in combination with pembrolizumab.

| Select warnings and precautions[2] | Incidence rates[2] | | Median time to onset (months)[2] |
|---|---|---|---|
| | All grades | Grade ≥3 | 0 6 12 18 24 MAX |
| Skin reactions | 70% | Grades 3-4: 17%*<br>Grade 5: 0.2% | 1.7 Severe skin reactions (range: 0.1 to 17.2) |
| Hyperglycemia[9] | 19%[9] | 9.2%[9] | 0.7 (range: 0 to 16.8)[9] |
| Pneumonitis/ILD | 10% | Grades 3-4: 4%<br>Grade 5: 0.4% | 4.0 (range: 0.3 to 26) |
| Peripheral neuropathy (PN) | 67% | Grade 3: 7% | 6.0 Grade ≥2 PN (range: 0.3 to 25) |
| Ocular disorders[9] | 31.9%[9] | 0 | — |
| Infusion site extravasation[9] | 1.6%[9] | 0.2%[9] | — |

Note: "–" indicates data is not available.

The bars represent the reported range of time to first onset of select ARs for patients who experienced that AR during clinical trials.

*These reactions included maculo-papular rash, bullous dermatitis, dermatitis, exfoliative dermatitis, pemphigoid, rash, erythematous rash, macular rash, and papular rash.[2]

**This is not a comprehensive list of ARs that have been reported in clinical trials of PADCEV. Hematologic toxicities and nonhematologic toxicities have been observed after administration of PADCEV. Please see the full Prescribing Information for a complete list.[2]**

**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

# 2L+ Incidence rates and median times to onset for select warnings and precautions for PADCEV® when given as monotherapy

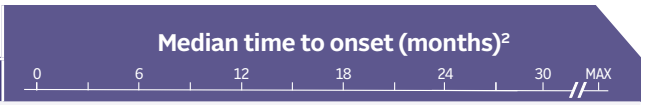
## Select warnings and precautions

**These data are not generalizable and cannot be used to predict AR outcomes. The AR information for PADCEV monotherapy describes ARs observed with exposure to PADCEV as a single agent at 1.25 mg/kg in 720 patients in EV-301, EV-201, EV-203, EV-101, and EV-102. Ocular disorders reflect 384 patients in EV-201, EV-101, and EV-102.[2]**

ARs associated with PADCEV may occur shortly after the initiation of treatment, which is why it is important to be attentive from the beginning.[2]

Evaluate your patients for ARs at each visit, as they may occur at any time during treatment with PADCEV.

| Select warnings and precautions[2] | Incidence rates[2] | | Median time to onset (months)[2] |
|---|---|---|---|
| | All grades | Grade ≥3 | |
| Skin reactions | 58% | 14%* | 0.6 Severe skin reactions (range: 0.1 to 8) |
| Hyperglycemia | 17% | Grades 3-4: 7%<br>Grade 5: 0.1% | 0.5 (range: 0 to 20) |
| Pneumonitis/ILD | 3% | 0.8% | 2.9 (range: 0.6 to 6) |
| Peripheral neuropathy (PN) | 53% | 5% | 4.9 Grade ≥2 PN (range: 0.1 to 20) |
| Ocular disorders | 40% | - | 1.7 (range: 0 to 30.6) |
| Infusion site extravasation | 1% | 0.3% | Generally immediately after administration, but possible delayed onset (eg, 24 hours) |




The bars represent the reported range of time to first onset of select ARs for patients who experienced that AR during clinical trials.

*These reactions included 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.[2]

**This is not a comprehensive list of ARs that have been reported in clinical trials of PADCEV. Hematologic toxicities and nonhematologic toxicities have been observed after administration of PADCEV. Please see the full Prescribing Information for a complete list.[2]**

**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

# Assessing patients and modifying PADCEV® dose

## ENCOURAGE PATIENTS TO IMMEDIATELY INFORM THEIR HEALTHCARE PROVIDER ABOUT ANY NEW OR WORSENING SIGNS OF SKIN REACTIONS[2]:

- Target lesions (skin reactions that look like rings)
- Rash or itching that continues to get worse
- Blistering or peeling of skin
- Painful sores or ulcers in mouth or nose, throat, or genital area
- Fever or flu-like symptoms
- Swollen lymph nodes

## POTENTIAL SCREENING QUESTIONS TO ASSIST IN IDENTIFICATION OF SKIN REACTIONS[2]

- Are you experiencing any new or worsening rashes, blistering, or peeling of skin?
- Have you had a fever or other flu-like symptoms?
- Have you noticed any sores or ulcers in your mouth, nose, throat, or genital area?

## PADCEV DOSE MODIFICATIONS FOR SKIN REACTIONS[2]

| SEVERITY* | PADCEV DOSE MODIFICATION* |
|---|---|
| For persistent or recurrent Grade 2 skin reactions | ■ **Consider withholding** until Grade ≤1<br>▫ Then **resume** treatment at the same dose level or dose reduce by one dose level |
| Grade 3 skin reactions | ■ **Withhold** until Grade ≤1<br>▫ 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.<br>If not SJS/TEN, see Grade 2-4 skin reactions |
| Confirmed SJS **or** TEN; Grade 4 **or** recurrent Grade 3 skin reactions | ■ **Permanently discontinue** |

■ WITHHOLD ■ RESUME ■ DISCONTINUE

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

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

**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

## CTCAE v6.0 grading scale for select skin reactions[10]

| CTCAE term | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| **Dry skin** | No associated erythema or pruritus | Associated with erythema or pruritus; limiting instrumental ADL* | — | — | — |
| **Erythema multiforme** | Not associated with skin tenderness | Associated with skin tenderness | Associated with oral or genital erosions | Associated with fluid or electrolyte abnormalities; ICU care or burn unit indicated | Death |
| **Pruritus** | Mild or localized; topical intervention indicated | Widespread and intermittent; skin changes from scratching (eg, edema, papulation, excoriations, lichenification, oozing/crusts); oral intervention indicated; limiting instrumental ADL* | Widespread and constant; systemic corticosteroid or immunosuppressive therapy indicated; limiting sleep or self-care ADL† | — | — |
| **Rash maculo-papular** | Asymptomatic | Mild symptoms | Macules/papules covering >50% BSA; moderate or severe symptoms | Life-threatening consequences; urgent intervention indicated | Death |
| **SJS** | — | — | Skin sloughing covering <10% BSA | Skin sloughing covering ≥10% BSA; life-threatening consequences | Death |
| **TEN** | — | — | — | Skin sloughing covering ≥30% BSA with associated symptoms (eg, erythema, purpura, or epidermal detachment); life-threatening consequences | Death |

Note: "—" indicates a grade is not available.
*Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
†Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications.

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

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

# Incidence, time to onset, and resolution in combination with pembrolizumab

**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.[2]**

## 1L Skin reactions in clinical trials of PADCEV in combination with pembrolizumab[2,9]

The combination data below are based on exposure to PADCEV in combination with pembrolizumab in EV-302 and EV-103. ARs were graded using National Cancer Institute CTCAE v4.03. [2,11,12]

| | In combination (N=564) | |
|---|---|---|
| | All grades | Grade 3-4 |
| Skin reactions (all types) | 70% | 17%* |
| Pruritus | 41.1% | 1.6% |
| Rash maculo-papular | 36% | 9.6% |

*Grade 3: 16%, Grade 4: 1%; these reactions included maculo-papular rash, bullous dermatitis, dermatitis, exfoliative dermatitis, pemphigoid, rash, erythematous rash, macular rash, and papular rash.[2]

| In combination | | |
|---|---|---|
| Median time to onset of **severe** skin reactions | **1.7** months | Range: 0.1 to 17.2 months |

The incidence of skin reactions, including severe events, occurred at a higher rate when PADCEV was given in combination with pembrolizumab. The majority of the skin reactions that occurred with combination therapy included maculo-papular rash, macular rash, and papular rash. A fatal reaction of bullous dermatitis occurred in one patient (0.2%).[2]

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.[2]

**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

# Incidence, time to onset, and resolution in monotherapy

## 2L+ Skin reactions in clinical trials of PADCEV® alone[2,6,9]

The data below are based on exposure to PADCEV as a single agent in EV-301, EV-201, EV-203, EV-101, and EV-102. ARs were graded using National Cancer Institute CTCAE v4.03.[2,6,9]

| | Monotherapy (N=720) | |
|---|---|---|
| | All grades | Grade 3-4 |
| Skin reactions (all types) | 58% | 14%* |
| Pruritus | 34% | 1.8% |
| Rash maculo-papular | 23% | 5.8% |

*These reactions included maculo-papular rash, erythematous rash, rash or drug eruption, SDRIFE, bullous dermatitis, exfoliative dermatitis, and palmar-plantar erythrodysesthesia.[2]

| Monotherapy | | |
|---|---|---|
| Median time to onset of **severe** skin reactions | **0.6** months | Range: 0.1 to 8 months |

In clinical trials of PADCEV as a single agent, 3.1% of patients discontinued PADCEV due to skin reactions. Among patients experiencing a skin reaction leading to dose interruption who then restarted PADCEV (n=75)[2]:

- 24% of patients restarting at the same dose experienced recurrent severe skin reactions
- 24% of patients restarting at a reduced dose experienced recurrent severe skin reactions

Of the patients who experienced a skin reaction and had data regarding resolution (n=328), 58% had complete resolution and 42% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 39% (53/137) had Grade ≥2 skin reactions.[2]

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

# Monitoring and clinical considerations

In combination therapy trials, of those who experienced a severe skin reaction, more than half of incidents occurred before the second month of treatment with PADCEV® in combination with pembrolizumab. In monotherapy clinical trials, of those who experienced a severe skin reaction, more than half of incidents occurred during the first treatment cycle with PADCEV.[2]

## CLINICAL CONSIDERATIONS FOR SKIN REACTIONS WHILE TREATING WITH PADCEV

Inform patients that severe skin reactions, including SJS and TEN, with fatal outcomes have occurred after administration of PADCEV, predominantly during the first cycle of treatment but may occur later. Educate patients on the potential for skin reactions, common signs or symptoms, and importance of immediately reporting[2]

**Withhold PADCEV and refer for specialized dermatology care for suspected SJS, TEN or for Grade 3 skin reactions.[2,12]**

Starting with the first cycle and throughout treatment, monitor patients for skin reactions[2]

Consider PADCEV dose modifications or appropriate treatment. As clinically indicated, consider topical corticosteroids and antihistamines[2]

## OTHER CONSIDERATIONS FOR TREATING SKIN REACTIONS WHILE ON ANTICANCER TREATMENTS[13]

**Treatment strategies for rash:**

- Applying fragrance-free, unscented, and hypoallergenic cream-based moisturizers to keep the area hydrated
- Consultation with their care team for specific recommendations on topical therapies, such as steroid creams or other anti-inflammatory ingredients
- Soaking in mixtures containing oatmeal, baking soda, or bath oil to help manage itchy or irritated skin
- Using cool cloths to help relieve pain and swelling

**General advice for skin care during and after cancer treatment may include:**

- Using mild soaps and skin cleansers
- Bathing with warm (not hot) water
- Applying sunscreen (SPF ≥30)
- Maintaining proper hydration
- Avoiding harsh chemicals that can irritate the skin

**These considerations come from professionals and organizations that support cancer care; they are not based on studies with PADCEV.**

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

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

# Assessing patients, modifying PADCEV® dose, and grading

## ENCOURAGE PATIENTS TO IMMEDIATELY INFORM THEIR HEALTHCARE PROVIDER ABOUT ANY NEW OR WORSENING SYMPTOMS OF HYPERGLYCEMIA[2]:

- Frequent urination
- Increased thirst
- Blurred vision
- Confusion
- Harder to control blood sugar
- Drowsiness
- Loss of appetite
- Fruity smell on breath
- Nausea
- Vomiting
- Stomach pain

## POTENTIAL SCREENING QUESTIONS TO ASSIST IN IDENTIFICATION OF HYPERGLYCEMIA[2]

- Have you recently experienced increased thirst, frequent urination, or difficulty controlling your blood sugar levels?
- Have you noticed blurred vision, confusion, or feeling unusually drowsy?
- Have you had nausea, vomiting, stomach pain, or a loss of appetite?
- Have you noticed a fruity smell on your breath?

## PADCEV DOSE MODIFICATIONS FOR HYPERGLYCEMIA[2]

| SEVERITY* | PADCEV DOSE MODIFICATION* |
|---|---|
| Blood glucose >250 mg/dL | ■ **Withhold** until elevated blood glucose has improved to ≤250 mg/dL<br>▫ Then **resume** treatment at the same dose level |

**WITHHOLD** **RESUME** **DISCONTINUE**

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

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

## CTCAE v6.0 grading scale for hyperglycemia[10]

| CTCAE term | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| **Hyperglycemia** | FBG >ULN-160 mg/dL | FBG >160 mg/dL-250 mg/dL | >250 mg/dL-500 mg/dL; hospitalization indicated | >500 mg/dL; life-threatening consequences | – |

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

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

# Incidence and time to onset

Patients with baseline HbA1c ≥8% were excluded from PADCEV® clinical trials.[2]

## 1L Hyperglycemia in clinical trials of PADCEV in combination with pembrolizumab[2,9]

The combination data below are based on exposure to PADCEV in combination with pembrolizumab in EV-302 and EV-103. ARs were graded using National Cancer Institute CTCAE v4.03.[2,11,12]

| | In combination (N=564) | |
|---|---|---|
| | All grades | Grade 3-4 |
| Hyperglycemia | 19% | 9.2% |

| In combination | | |
|---|---|---|
| Median time to onset of hyperglycemia | 0.7 months | Range: 0 to 16.8 months |

## 2L+ Hyperglycemia in clinical trials of PADCEV alone[2]

Hyperglycemia and diabetic ketoacidosis (DKA), including fatal events, occurred in patients with and without preexisting diabetes mellitus treated with PADCEV. Fatal events of hyperglycemia and diabetic ketoacidosis occurred in one patient each (0.1%).[2]

The data below are based on exposure to PADCEV as a single agent in EV-301, EV-201, EV-203, EV-101, and EV-102. ARs were graded using National Cancer Institute CTCAE v4.03.[2,6,9]

| | Monotherapy (N=720) | |
|---|---|---|
| | All grades | Grade 3-4 |
| Hyperglycemia | 17% | 7% |

| Monotherapy | | |
|---|---|---|
| Median time to onset of hyperglycemia | 0.5 months | Range: 0 to 20 months |

The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher BMI and in patients with higher baseline HbA1c. 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. Hyperglycemia led to discontinuation of PADCEV in 0.7% of patients.[2]

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

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

# Monitoring and clinical considerations

## Risk factors for hyperglycemia

In clinical trials of PADCEV® as a single agent, Grade 3-4 hyperglycemia increased consistently in patients with higher BMI and higher baseline HbA1c[2]

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

### CONSIDERATIONS FOR HYPERGLYCEMIA WHILE ON PADCEV

Educate patients on the potential for hyperglycemia, common signs or symptoms, and importance of early reporting[2]

Assess baseline HbA1c measurement before starting PADCEV. Patients with baseline hemoglobin A1C ≥8% were excluded from clinical trials[2]

Routinely monitor blood glucose levels prior to each PADCEV dose. If blood glucose is elevated (>250 mg/dL), withhold PADCEV until elevated blood glucose has improved to ≤250 mg/dL[2]

Patients with a history of high blood sugar or diabetes should inform their primary healthcare professional about their treatment with PADCEV

- If elevated HbA1c ≥6.5% is identified at screening, referral to a provider for glucose management is appropriate[2,12]

**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

# Assessing patients, modifying PADCEV® dose, grading, and monitoring

## ENCOURAGE PATIENTS TO IMMEDIATELY INFORM THEIR HEALTHCARE PROVIDER ABOUT ANY NEW OR WORSENING SYMPTOMS OF PNEUMONITIS/ILD[2]:

- Trouble breathing
- Cough
- Shortness of breath

## POTENTIAL SCREENING QUESTIONS TO ASSIST IN IDENTIFICATION OF PNEUMONITIS/ILD[2]

- Have you experienced any coughing or shortness of breath?
- Are you experiencing any trouble breathing during your usual activities?

## PADCEV DOSE MODIFICATIONS FOR PNEUMONITIS/ILD[2]

| SEVERITY* | PADCEV DOSE MODIFICATION* |
|---|---|
| Grade 2 | ■ **Withhold** until Grade ≤1<br>▫ Then **resume** treatment at the same dose level or consider dose reduction by one dose level |
| Grade ≥3 | ■ **Permanently discontinue** |

■ WITHHOLD ■ RESUME ■ DISCONTINUE

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

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

## CTCAE v6.0 grading scale for pneumonitis[10]

| CTCAE term | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| **Pneumonitis** | Asymptomatic; clinical or diagnostic observations only; intervention not indicated | Symptomatic; medical intervention indicated; limiting instrumental ADL† | Severe symptoms; oxygen indicated; limiting self-care ADL‡ | Life-threatening respiratory compromise; urgent intervention indicated (eg, tracheotomy or intubation) | Death |

†Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
‡Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications.

## Monitoring for pneumonitis/ILD[2]

- 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

**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

# Incidence and time to onset

Severe, life-threatening, or fatal pneumonitis/ILD occurred in patients treated with PADCEV®.[2]

## 1L Pneumonitis/ILD in clinical trials of PADCEV in combination with pembrolizumab[2]

The combination data below are based on exposure to PADCEV in combination with pembrolizumab in EV-302 and EV-103. ARs were graded using National Cancer Institute CTCAE v4.03.[2,11,12]

| | In combination (N=564) | |
|---|---|---|
| | All grades | Grade 3-4 |
| Pneumonitis/ILD | 10% | 4% |

| | | |
|---|---|---|
| In combination Median time to onset of pneumonitis/ILD | 4 months | Range: 0.3 to 26 months |

The incidence of pneumonitis/ILD, including severe events, occurred at a higher rate when PADCEV was given in combination with pembrolizumab. A fatal event of pneumonitis/ILD occurred in 2 patients (0.4%).[2]

## 2L+ Pneumonitis/ILD in clinical trials of PADCEV alone[2]

The data below are based on exposure to PADCEV as a single agent in EV-301, EV-201, EV-203, EV-101, and EV-102. ARs were graded using National Cancer Institute CTCAE v4.03.[2,6,9]

| | Monotherapy (N=720) | |
|---|---|---|
| | All grades | Grade 3-4 |
| Pneumonitis/ILD | 3% | 0.8% |

| | | |
|---|---|---|
| Monotherapy Median time to onset of pneumonitis/ILD | 2.9 months | Range: 0.6 to 6 months |

**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

# Assessing patients, modifying PADCEV® dose, and grading

## ENCOURAGE PATIENTS TO IMMEDIATELY INFORM THEIR HEALTHCARE PROVIDER ABOUT ANY NEW OR WORSENING SYMPTOMS OF PN[2]:

- Numbness in hands or feet
- Tingling in the hands or feet
- Muscle weakness

## POTENTIAL SCREENING QUESTIONS TO ASSIST IN IDENTIFICATION OF PN[2]

- Have you noticed any new or worsening numbness or tingling in your hands or feet?
- Are you experiencing any muscle weakness?

## PADCEV DOSE MODIFICATIONS FOR PN[2]

| SEVERITY* | PADCEV DOSE MODIFICATION* |
|---|---|
| Grade 2 | ■ **Withhold** until Grade ≤1<br>▫ Then **resume** treatment at the same dose level (if first occurrence)<br>■ For a recurrence, **withhold** until Grade ≤1<br>▫ Then **resume** treatment reduced by one dose level |
| Grade ≥3 | ■ **Permanently discontinue** |

■ WITHHOLD ■ RESUME ■ DISCONTINUE

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

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

## CTCAE v6.0 grading scale for select types of PN[10]

| CTCAE term | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| **Peripheral motor neuropathy** | Mild symptoms; clinical or diagnostic observations only | Moderate symptoms; limiting instrumental ADL† | Severe symptoms; limiting self-care ADL‡ | Life-threatening consequences; urgent intervention indicated | Death |
| **Peripheral sensory neuropathy** | Mild symptoms | Moderate symptoms; limiting instrumental ADL† | Severe symptoms; limiting self-care ADL‡ | Life-threatening consequences; urgent intervention indicated | — |

Note: "—" indicates a grade is not available.
†Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
‡Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications.

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

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

# Incidence and time to onset

PN occurred in patients treated with PADCEV® with or without preexisting peripheral neuropathy. Monitor patients for symptoms of new or worsening peripheral neuropathy and consider dose interruption, dose reduction, or discontinuation of PADCEV when PN occurs.[2]

## 1L PN in clinical trials of PADCEV in combination with pembrolizumab[2]

The combination data below are based on exposure to PADCEV in combination with pembrolizumab in EV-302 and EV-103. ARs were graded using National Cancer Institute CTCAE v4.03.[2,11,12]

| | In combination (N=564) | | |
|---|---|---|---|
| | All grades | Grade 2 | Grade 3 |
| Incidence of PN | 67% | 36% | 7% |

| | | |
|---|---|---|
| In combination<br>Median time to onset of PN (Grade ≥2) | 6 months | Range: 0.3 to 25 months |

The incidence of PN occurred at a higher rate when PADCEV was given in combination with pembrolizumab.[2]

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.[2]

## 2L+ PN in clinical trials of PADCEV alone[2]

The data below are based on exposure to PADCEV as a single agent in EV-301, EV-201, EV-203, EV-101, and EV-102. ARs were graded using National Cancer Institute CTCAE v4.03.[2,6,9]

| | Monotherapy (N=720) | | |
|---|---|---|---|
| | All grades | Grade 2 | Grade 3-4 |
| Incidence of PN | 53%* | 30% | 5% |

| | | |
|---|---|---|
| Monotherapy<br>Median time to onset of PN (Grade ≥2) | 4.9 months | Range: 0.1 to 20 months |

In monotherapy clinical trials, PN led to treatment discontinuation in 6% of patients.[2]

Of the patients who experienced neuropathy who had data regarding resolution (n=296), 11% had complete resolution, and 89% had residual neuropathy at the time of their last evaluation. Of the patients with residual neuropathy at last evaluation, 50% (132/262) had Grade ≥2 neuropathy.[2]

*38% had sensory neuropathy, 8% had muscular weakness, and 7% had motor neuropathy.[2]

**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 considerations

## CLINICAL CONSIDERATIONS FOR PN WHILE TREATING WITH PADCEV®

- Closely monitor patients for signs and symptoms of new or worsening PN[2]
- Consider dose interruption, dose reduction, or discontinuation of PADCEV when PN occurs (**click here for dose modifications**)[2]
- Inform patients to report to their healthcare provider any numbness and tingling of the hands or feet or muscle weakness[2]

## OTHER CONSIDERATIONS FOR PN WHILE ON ANTICANCER TREATMENTS[14]

- In order to avoid injuries and worsening symptoms, advise patients not to bring their bare hands or feet into direct contact with hot or cold items. Also, recommend that patients wear clothes and shoes that are not too tight.
- Consider recommending wearing shoes at all times when walking to protect the feet, and regular self-examination of feet for injury or open sores

**These considerations come from professionals and organizations that support cancer care; they have not been studied with PADCEV.**

**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

# Assessing patients, modifying PADCEV® dose, and clinical considerations

Ocular disorders involving the cornea and included events associated with dry eye such as keratitis, blurred vision, increased lacrimation, conjunctivitis, limbal stem cell deficiency, and keratopathy, have been reported with treatment with PADCEV.

## ENCOURAGE PATIENTS TO IMMEDIATELY INFORM THEIR HEALTHCARE PROVIDER ABOUT ANY NEW OR WORSENING SYMPTOMS OF OCULAR DISORDERS[2]:

- Dry eyes
- Blurred vision
- Increased tearing
- Any vision changes

## POTENTIAL SCREENING QUESTIONS TO ASSIST IN IDENTIFICATION OF OCULAR DISORDERS[2]

- Have you noticed any changes in your vision, such as blurriness or other visual disturbances?
- Are you experiencing issues with your eyes, like dryness or excessive tearing?

## PADCEV DOSE MODIFICATIONS FOR OCULAR DISORDERS[2]

| PADCEV DOSE MODIFICATION |
|---|
| ▪ **Consider dose interruption** or dose reduction of PADCEV for symptomatic ocular disorders |

WITHHOLD RESUME DISCONTINUE

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

## CLINICAL CONSIDERATIONS FOR OCULAR DISORDERS WHILE TREATING WITH PADCEV

- Monitor patients for ocular disorders. Consider artificial tears for prophylaxis of dry eyes and ophthalmologic evaluation if ocular symptoms occur or do not resolve[2]
- Consider treatment with ophthalmic topical steroids, if indicated after an ophthalmic exam[2]
- Consider advising patients about the potential for ocular disorders, including dry eyes and blurred vision, and instruct them to contact their healthcare provider if they experience any visual changes[2]
- If ocular symptoms and/or changes in vision are identified, the patient should be evaluated by an optometrist or ophthalmologist[1,2]

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

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

## CTCAE v6.0 grading scale for select ocular disorders[10]

| CTCAE term | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| **Blurred vision** | Intervention not indicated | Symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better or 3 lines or less decreased vision from known baseline); limiting instrumental ADL* | Symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or more than 3 lines of decreased vision from known baseline, up to 20/200); limiting self-care ADL† | Best corrected visual acuity of 20/200 or worse in the affected eye | — |
| **Dry eye** | Clinical or diagnostic observations only; symptoms relieved by lubricants | Symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better or 3 lines or less decreased vision from known baseline) | Symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or more than 3 lines of decreased vision from known baseline, up to 20/200); limiting self-care ADL† | — | — |
| **Keratitis** | Asymptomatic; clinical or diagnostic observations only; intervention not indicated | Symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better or 3 lines or less decreased vision from known baseline) | Symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or more than 3 lines of decreased vision from known baseline, up to 20/200); corneal ulcer; limiting self-care ADL† | Perforation; best corrected visual acuity of 20/200 or worse in the affected eye | — |

Note: "—" indicates a grade is not available.

*Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
†Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications.

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

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

# Incidence and time to onset

## 1L Ocular disorders in clinical trials of PADCEV® in combination with pembrolizumab[9]

The combination data below are based on exposure to PADCEV in combination with pembrolizumab in EV-302 and EV-103. Adverse reactions (ARs) were graded using National Cancer Institute CTCAE v4.03.[2,11,12]

| | In combination (N=564) |
|---|---|
| | Incidence rate (Grade 1-2) |
| All types | 31.9% |
| Dry eye | 27.7% |

## 2L+ Ocular disorders in clinical trials of PADCEV alone[2]*

Ocular disorders have occurred in patients treated with PADCEV in clinical trials. 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.[2]

The data below are based on exposure to PADCEV as a single agent in EV-201, EV-101, and EV-102. ARs were graded using National Cancer Institute CTCAE v4.03.[2,9]

| | Monotherapy (N=384) |
|---|---|
| | Incidence rate (all grades) |
| All types | 40% |
| Dry eye | 30% |
| Blurred vision | 10% |

| Monotherapy | | |
|---|---|---|
| Median time to onset of ocular disorders | 1.7 months | Range: 0 to 30.6 months |

*Ophthalmologic exams were scheduled in 384 patients treated with PADCEV as a single agent in clinical trials.[2]

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

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

# Grading, clinical considerations, and incidence

## CTCAE v6.0 grading scale for infusion site extravasation[10]

| CTCAE term | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| **Infusion site extravasation** | Painless edema | Erythema with associated symptoms (eg, edema, pain, induration, phlebitis) | Ulceration or necrosis; severe tissue damage; operative intervention indicated | Life-threatening consequences; urgent intervention indicated | Death |

## CLINICAL CONSIDERATIONS FOR TREATING WITH PADCEV®[2]

- 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
- 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 healthcare professional immediately if they experience any symptoms of an infusion site reaction

## 1L Infusion site extravasation in clinical trials of PADCEV in combination with pembrolizumab[9]

The combination data below are based on exposure to PADCEV in combination with pembrolizumab in EV-302 and EV-103. ARs were graded using National Cancer Institute CTCAE v4.03.[2,11,12]

| | In combination (N=564) | |
|---|---|---|
| | All grades | Grade 3-4 |
| Infusion site extravasation | 1.6% | 0.2% |

## 2L+ Skin and soft tissue reactions secondary to infusion site extravasation in clinical trials of PADCEV alone[2]

The data below are based on exposure to PADCEV as a single agent in EV-301, EV-201, EV-203, EV-101, and EV-102. ARs were graded using National Cancer Institute CTCAE v4.03.[2,6,9]

| | Monotherapy (N=720) | |
|---|---|---|
| | All grades | Grade 3-4 |
| Infusion site extravasation | 1% | 0.3% |

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.[2]

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

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

# Assessing and grading

For a list of the most common GI disorders that occurred in patients taking PADCEV® in combination with pembrolizumab in the EV-302 clinical trial, **click here**.
For a list of the most common GI disorders that occurred in patients taking PADCEV as a single agent in the EV-301 and EV-201 Cohort 2 clinical trials, **click here**.

## ENCOURAGE PATIENTS TO IMMEDIATELY INFORM THEIR HEALTHCARE PROVIDER ABOUT ANY NEW OR WORSENING SYMPTOMS OF GI DISORDERS[2]:

- Diarrhea
- Nausea
- Constipation
- Abdominal pain
- Decreased appetite
- Decreased weight

## POTENTIAL SCREENING QUESTIONS TO ASSIST IN IDENTIFICATION OF GI DISORDERS[2]

- Have you been experiencing any digestive issues, such as diarrhea, constipation, or nausea?
- Have you noticed any appetite loss?

## CTCAE v6.0 grading scale for select GI disorders[10]

| CTCAE term | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| **Constipation** | Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema | Persistent symptoms with regular use of laxatives or enemas; limiting instrumental ADL* | Obstipation with manual evacuation indicated; limiting self-care ADL† | Life-threatening consequences; urgent intervention indicated | Death |
| **Diarrhea** | Change in consistency or frequency | Increase of 4-6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL*; change in consistency or frequency | Increase of ≥7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; requires IV intervention; limiting self-care ADL† | Life-threatening consequences; urgent intervention indicated | Death |
| **Nausea** | Loss of appetite without alteration in eating habits | Oral intake decreased without significant weight loss, dehydration, or malnutrition; IV intervention indicated | Inadequate oral caloric or fluid intake; tube feeding, total parenteral nutrition, or hospitalization indicated | — | — |

Note: "—" indicates a grade is not available.
*Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
†Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications.

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

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

# Modifying PADCEV® dose and clinical considerations

## PADCEV DOSE MODIFICATIONS FOR NONHEMATOLOGIC TOXICITY[2]

| SEVERITY* | PADCEV DOSE MODIFICATION* |
|---|---|
| Grade 3 | ■ **Withhold** until Grade ≤1<br>▫ Then **resume** treatment at the same dose level or consider dose reduction by one dose level |
| Grade 4 | ■ **Permanently discontinue** |

■ WITHHOLD ■ RESUME ■ DISCONTINUE

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

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

## CONSIDERATIONS FOR GI DISORDERS WHILE ON ANTICANCER TREATMENTS[15]

- Try the BRAT (bananas, rice, applesauce, toast) diet while experiencing diarrhea
- Adequate oral hydration with reduced appetite, oral intake, and/or diarrhea
- Perform pharmacologic management of nausea and diarrhea (if clinically indicated)
- Consider nutrition consultation, as indicated
- Patient education on potential for problems with nutrition
- Adequate nutrition and hydration may support recovery by helping maintain strength, energy, and body weight
- For taste alterations† and appetite changes‡, consider supportive care strategies such as:
  - Using lemon juice and chewing gum prior to meals
  - Having small, frequent meals
  - Good oral hygiene
  - Drinking water with meals
  - Using plastic instead of metal utensils
  - Using more/less salt and flavoring for food
  - Avoiding food with strong smells

**These considerations come from professionals and organizations that support cancer care; they have not been studied with PADCEV.**

†EV clinical trials classify taste changes or dysgeusia based on MedDRA as a nervous system disorder.[2]
‡EV clinical trials classify reduced or decreased appetite based on MedDRA as a metabolism and nutrition disorder.[2]

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

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

# Modifying PADCEV® dose, grading, and clinical considerations

For a list of the most common hematologic laboratory abnormalities that occurred in patients taking PADCEV in combination with pembrolizumab in the EV-302 clinical trial, click here. For a list of the most common hematologic laboratory abnormalities that occurred in patients taking PADCEV as a single agent in the EV-301 and EV-201 Cohort 2 clinical trials, click here.

## PADCEV DOSE MODIFICATIONS FOR HEMATOLOGIC TOXICITY[2]

| SEVERITY* | PADCEV DOSE MODIFICATION* |
|---|---|
| Grade 3, or Grade 2 thrombocytopenia | ■ **Withhold** until Grade ≤1<br>▫ Then **resume** treatment at the same dose level or consider dose reduction by one dose level |
| Grade 4 | ■ **Withhold** until Grade ≤1<br>▫ Then reduce dose by one dose level or **discontinue treatment** |

■ WITHHOLD ■ RESUME ■ DISCONTINUE

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

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

## CTCAE v6.0 grading scale for select hematologic toxicities[10]

| CTCAE term | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| **Anemia** | Hgb<br><LLN-10.0 g/dL | Hgb<br><10.0-8.0 g/dL | Hgb<br><8.0 g/dL;<br>transfusion indicated | Life-threatening consequences;<br>urgent intervention indicated | Death |
| **Neutrophil count decreased** | <1500-1000/mm$^3$;<br><1.5-1 x 10$^9$/L | <1000-500/mm$^3$;<br><1.0-0.5 x 10$^9$/L | <500-100/mm$^3$;<br><0.5-0.1 x 10$^9$/L | <100/mm$^3$;<br><0.1 x 10$^9$/L | — |

Note: "—" indicates a grade is not available.

## CONSIDERATIONS FOR HEMATOLOGIC TOXICITIES WHILE ON PADCEV[2,12]

The detection of hematologic laboratory abnormalities, such as anemia, neutropenia, and thrombocytopenia, requires regular monitoring

## CONSIDERATIONS FOR HEMATOLOGIC TOXICITIES WHILE ON ANTICANCER TREATMENTS[16,17]

Communicate the importance of frequent hand hygiene

Consider advising patients to use a thermometer at home and immediately report a temperature of 100.4°F or greater

**These considerations come from professionals and organizations that support cancer care; they have not been studied with PADCEV.**

**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

# Adverse reactions in the EV-302 clinical trial (previously untreated patients)[2]

| Adverse Reactions, %<br>Reported in ≥15% (all grades) of patients treated with PADCEV® in combination with pembrolizumab[2] | PADCEV IN COMBINATION WITH PEMBROLIZUMAB (n=440) | | CHEMOTHERAPY (n=433) | |
|---|---|---|---|---|
| | ALL GRADES* | GRADE 3-4 | ALL GRADES* | GRADE 3-4 |
| **Skin and subcutaneous tissue disorders** | | | | |
| Rash† | 68 | 15 | 15 | 0 |
| Pruritus | 41 | 1.1 | 7 | 0 |
| Alopecia | 35 | 0.5 | 8 | 0.2 |
| Dry skin | 17 | 0.2 | 1 | 0 |
| **General disorders and administration site conditions** | | | | |
| Fatigue† | 51 | 6 | 57 | 7 |
| Pyrexia | 18 | 0.7 | 16 | 1.2 |
| **Nervous system disorders** | | | | |
| Peripheral neuropathy† | 67 | 8 | 14 | 0 |
| Dysgeusia | 21 | 0 | 9 | 0 |
| **Metabolism and nutrition disorders** | | | | |
| Decreased appetite | 33 | 1.8 | 26 | 1.8 |
| **Gastrointestinal disorders** | | | | |
| Diarrhea | 38 | 4.5 | 16 | 1.4 |
| Nausea | 26 | 1.6 | 41 | 2.8 |
| Constipation | 26 | 0 | 34 | 0.7 |
| **Investigations** | | | | |
| Decreased weight | 33 | 3.6 | 9 | 0.2 |
| **Eye disorders** | | | | |
| Dry eye† | 24 | 0 | 2.1 | 0 |
| **Infections and infestations** | | | | |
| Urinary tract infection | 21 | 5 | 19 | 8 |

*Graded per NCI CTCAE v4.03.
†Includes multiple terms.

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

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

# Laboratory abnormalities in the EV-302 clinical trial[2]

## Selected Laboratory Abnormalities

Reported in ≥15% (all grades) of patients treated with PADCEV® in combination with pembrolizumab[2]

| | PADCEV IN COMBINATION WITH PEMBROLIZUMAB | | CHEMOTHERAPY | |
|---|---|---|---|---|
| LABORATORY ABNORMALITY, %* | ALL GRADES† | GRADE 3-4 | ALL GRADES† | GRADE 3-4 |
| **Chemistry** | | | | |
| Increased aspartate aminotransferase | 75 | 5 | 39 | 3 |
| Increased creatinine | 71 | 3 | 68 | 3 |
| Increased glucose | 66 | 14 | 54 | 5 |
| Increased alanine aminotransferase | 59 | 5 | 49 | 3 |
| Decreased sodium | 46 | 13 | 47 | 13 |
| Decreased phosphate | 44 | 9 | 36 | 9 |
| Decreased albumin | 39 | 2 | 35 | 0.5 |
| Decreased potassium | 26 | 5 | 16 | 3 |
| Increased potassium | 24 | 1 | 36 | 4 |
| Increased calcium | 21 | 1 | 14 | 0.2 |
| **Hematology** | | | | |
| Decreased lymphocytes | 58 | 15 | 59 | 17 |
| Decreased hemoglobin | 53 | 7 | 89 | 33 |
| Decreased neutrophils | 30 | 9 | 80 | 50 |

- Median duration of exposure to PADCEV was 7 months (range: 0.3 to 31.9 months)[2]
- Serious adverse reactions occurred in 50% of patients treated with PADCEV in combination with 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%)[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%)[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 peripheral neuropathy (15%), rash (4.1%), and pneumonitis/ILD (2.3%)[2]
- **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 peripheral neuropathy (22%), rash (16%), COVID-19 (10%), diarrhea (5%), pneumonitis/ILD (4.8%), fatigue (3.9%), hyperglycemia (3.6%), increased alanine aminotransferase (3%), and pruritus (2.5%)[2]
- **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%), peripheral neuropathy (13%), and fatigue (2.7%)[2]

*The denominator used to calculate the rate varied from 407 to 439 based on the number of patients with a baseline value and at least one post-treatment value.[2]
†Graded per NCI CTCAE v4.03.[2]

**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

# Adverse reactions in the EV-301 clinical trial (post-platinum, post–PD-(L)1 patients)[2]

| Adverse Reactions, % (≥15%) in patients treated with PADCEV®[2] | PADCEV (n=296) | | CHEMOTHERAPY (n=291) | |
|---|---|---|---|---|
| | ALL GRADES* | GRADE 3-4 | ALL GRADES* | GRADE 3-4 |
| **Skin and subcutaneous tissue disorders** | | | | |
| Rash† | 54 | 14 | 20 | 0.3 |
| Alopecia | 47 | 0 | 38 | 0 |
| Pruritus | 34 | 2 | 7 | 0 |
| Dry skin | 17 | 0 | 4 | 0 |
| **General disorders and administration site conditions** | | | | |
| Fatigue† | 50 | 9 | 40 | 7 |
| Pyrexia† | 22 | 2 | 14 | 0 |
| **Nervous system disorders** | | | | |
| Peripheral neuropathy† | 50 | 5 | 34 | 3 |
| Dysgeusia† | 26 | 0 | 8 | 0 |
| **Metabolism and nutrition disorders** | | | | |
| Decreased appetite | 41 | 5 | 27 | 2 |
| **Gastrointestinal disorders** | | | | |
| Diarrhea† | 35 | 4 | 23 | 2 |
| Nausea | 30 | 1 | 25 | 2 |
| Constipation | 28 | 1 | 25 | 2 |
| Abdominal pain† | 20 | 1 | 14 | 3 |
| **Musculoskeletal and connective tissue disorders** | | | | |
| Musculoskeletal pain† | 25 | 2 | 35 | 5 |
| **Eye disorders** | | | | |
| Dry eye† | 24 | 0.7 | 6 | 0.3 |
| **Infections and infestations** | | | | |
| Urinary tract infection† | 17 | 6 | 13 | 3 |
| **Vascular disorders** | | | | |
| Hemorrhage† | 17 | 3 | 13 | 2 |
| **Investigations** | | | | |
| Decreased weight | 16 | 0.3 | 7 | 0 |

*Graded per NCI CTCAE v4.03.
†Includes multiple terms.

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

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

# Laboratory abnormalities in the EV-301 clinical trial[2]

| Selected Laboratory Abnormalities<br>Reported in ≥15% (Grades 2-4) or ≥5% (Grade 3-4) of patients treated with PADCEV®[2] | PADCEV | | CHEMOTHERAPY | |
|---|---|---|---|---|
| **LABORATORY ABNORMALITY, %*** | **GRADES 2-4†** | **GRADE 3-4** | **GRADES 2-4†** | **GRADE 3-4** |
| **Hematology** | | | | |
| Decreased lymphocytes | 41 | 14 | 34 | 18 |
| Decreased hemoglobin | 28 | 4 | 42 | 14 |
| Decreased neutrophils | 27 | 12 | 25 | 17 |
| **Chemistry** | | | | |
| Decreased phosphate | 39 | 8 | 24 | 6 |
| Increased glucose (non-fasting) | 33 | 9 | 27 | 6 |
| Increased creatinine | 18 | 2 | 13 | 0 |
| Decreased potassium | 16 | 2 | 7 | 3 |
| Increased lipase | 13 | 8 | 7 | 4 |
| Decreased sodium | 8 | 8 | 5 | 5 |

- The median duration of exposure to PADCEV was 5 months (range: 0.5 to 19 months)[2]
- Serious adverse reactions occurred in 47% of patients treated with PADCEV. The most common serious adverse reactions (≥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)[2]
- **Adverse reactions leading to discontinuation** occurred in 17% of patients; the most common adverse reactions (≥2%) leading to discontinuation were peripheral neuropathy (5%) and rash (4%)[2]
- **Adverse reactions leading to dose interruption** occurred in 61% of patients; the most common adverse reactions (≥4%) leading to dose interruption were peripheral neuropathy (23%), rash (11%), and fatigue (9%)[2]
- **Adverse reactions leading to dose reduction** occurred in 34% of patients; the most common adverse reactions (≥2%) leading to dose reduction were peripheral neuropathy (10%), rash (8%), decreased appetite (3%), and fatigue (3%)[2]

*The denominator used to calculate the rate varied from 262 to 287 based on the number of patients with a baseline value and at least one post-treatment value.[2]
†Graded per NCI CTCAE v4.03.[2]

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

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

# Adverse reactions in the EV-201, Cohort 2 trial (cisplatin-ineligible, post–PD-(L)1 patients)[2]

| Adverse Reactions, %<br>≥15% (all grades) or ≥5% (Grades 3-4) of patients treated with PADCEV®[2] | PADCEV (n=89) | |
|---|---|---|
| **ADVERSE REACTION, %** | **ALL GRADES*** | **GRADES 3-4** |
| **Skin and subcutaneous tissue disorders** | | |
| Rash† | 66 | 17 |
| Alopecia | 53 | 0 |
| Pruritus | 35 | 3 |
| Dry skin | 19 | 1 |
| **Nervous system disorders** | | |
| Peripheral neuropathy† | 58 | 8 |
| Dysgeusia† | 29 | 0 |
| **General disorders and administration site conditions** | | |
| Fatigue† | 48 | 11 |
| **Metabolism and nutrition disorders** | | |
| Decreased appetite | 40 | 6 |
| Hyperglycemia | 16 | 9 |
| **Gastrointestinal disorders** | | |
| Diarrhea† | 36 | 8 |
| Nausea | 30 | 1 |
| **Investigations** | | |
| Decreased weight | 35 | 1 |
| **Eye disorders** | | |
| Dry eye† | 30 | 0 |

*Graded per NCI CTCAE v4.03.
†Includes multiple terms.

**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

# Laboratory abnormalities in the EV-201, Cohort 2 trial[2]

| Selected Laboratory Abnormalities<br>Reported in ≥15% (Grades 2-4) or ≥5% (Grades 3-4) of patients treated with PADCEV®[2] | PADCEV (n=88) | |
|---|---|---|
| **LABORATORY ABNORMALITY, %*** | **GRADES 2-4†** | **GRADES 3-4** |
| **Hematology** | | |
| Decreased lymphocytes | 43 | 15 |
| Decreased hemoglobin | 34 | 5 |
| Decreased neutrophils | 20 | 9 |
| **Chemistry** | | |
| Increased glucose (non-fasting) | 36 | 13 |
| Decreased phosphate | 25 | 7 |
| Increased creatinine | 23 | 3 |
| Increased lipase | 18 | 11 |
| Increased urate | 9 | 9 |
| Increased potassium | 8 | 6 |
| Decreased sodium | 7 | 7 |

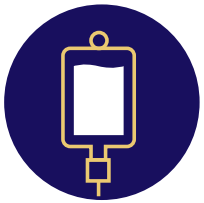
- The median duration of exposure was 5.98 months (range: 0.3 to 24.6 months)[2]
- Serious adverse reactions occurred in 39% of patients treated with PADCEV. The most common serious adverse reactions (≥3%) were pneumonia, sepsis, and diarrhea (5% each). Fatal adverse reactions occurred in 8% of patients, including acute kidney injury (2.2%), metabolic acidosis, sepsis, multiorgan dysfunction, pneumonia, and pneumonitis/ILD (1.1% each)[2]
- **Adverse reactions leading to discontinuation** occurred in 20% of patients; the most common adverse reaction (≥2%) leading to discontinuation was peripheral neuropathy (7%)[2]
- **Adverse reactions leading to dose interruption** occurred in 60% of patients; the most common adverse reactions (≥3%) leading to dose interruption were peripheral neuropathy (19%), rash (9%), fatigue (8%), diarrhea (5%), increased aspartate aminotransferase (3%), and hyperglycemia (3%)[2]
- **Adverse reactions leading to dose reduction** occurred in 49% of patients; the most common adverse reactions (≥3%) leading to dose reduction were peripheral neuropathy (19%), rash (11%), and fatigue (7%)[2]

*Based on the number of patients with a baseline value and at least one post-treatment value.[2]
†Graded per NCI CTCAE v4.03.[2]

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

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

# ADDITIONAL RESOURCES FOR PATIENTS AND HEALTHCARE TEAM



### Dosing and Administration Guide

This reference guide provides information about PADCEV® recommended dosing, dose modifications due to ARs, and preparation and administration.

### AR Monitoring Checklist

This tool helps you track the signs and symptoms of ARs your patients may experience during treatment with PADCEV.

### Patient Symptom Tracker

This resource can help patients and their caregivers track potential ARs that may occur with PADCEV treatment.

**Contact your Astellas/Pfizer representative for copies of these resources and others, or visit PADCEVhcp.com/resources to download them directly.**

For more information, call 1-888-4PADCEV (1-888-472-3238) or visit PADCEVhcp.com.

**ADL**=activities of daily living; **BICR**=blinded independent central review; **BMI**=body mass index; **BSA**=body surface area; **CI**=confidence interval; **CR**=complete response; **ECOG PS**=Eastern Cooperative Oncology Group performance status; **FBG**=fasting blood glucose; **GI**=gastrointestinal; **HbA1c**=hemoglobin A1c; **Hgb**=hemoglobin; **HR**=hazard ratio; **ICU**=intensive care unit; **ILD**=interstitial lung disease; **IV**=intravenous; **LLN**=lower limit of normal; **MedDRA**=Medical Dictionary for Regulatory Activities; **mOS**=median overall survival; **mPFS**=median progression-free survival; **mUC**=metastatic urothelial cancer; **NCI CTCAE**=National Cancer Institute Common Terminology Criteria for Adverse Events; **NE**=not estimable; **OS**=overall survival; **PD-(L)1**=programmed death receptor-1 or programmed death-ligand 1; **PFS**=progression-free survival; **PR**=partial response; **RECIST**=Response Evaluation Criteria in Solid Tumors; **SJS**=Stevens-Johnson syndrome; **SPF**=sun protection factor; **TEN**=toxic epidermal necrolysis; **ULN**=upper limit of normal.

**References: 1.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.3.2026. © National Comprehensive Cancer Network, Inc. 2026. All rights reserved. Accessed August 6, 2026. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2.** PADCEV. Package insert. Northbrook, IL: Astellas Pharma US, Inc; 2026. **3.** 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. **4.** Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. *N Engl J Med*. 2021;384(12):1125–1135. **5.** Supplement to: Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. *N Engl J Med*. 2021;384(12):1125–1135. **6.** Protocol for: Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. *N Engl J Med*. 2021;384(12):1125–1135. **7.** Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer*. 2009;45(2):228–247. **8.** Keytruda. Package insert. Rahway, NJ: Merck Sharp & Dohme LLC; 2026. **9.** Pfizer Inc. and Astellas. PADCEV. Data on File. **10.** U.S. Department of Health and Human Services. Cancer Therapy Evaluation Program. Common Terminology Criteria for Adverse Events (CTCAE) v6.0 (MedDRA 28.0). Published July 22, 2025. Accessed October 8, 2025. https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v6.pdf. **11.** Protocol for: O'Donnell PH, Milowsky MI, Petrylak DP, et al. Enfortumab vedotin with or without pembrolizumab in cisplatin-ineligible patients with previously untreated locally advanced or metastatic urothelial cancer. *J Clin Oncol*. 2023;41(25):4107–4117. **12.** 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. **13.** American Cancer Society. Rashes and skin changes. Updated September 12, 2024. Accessed May 9, 2025. https://www.cancer.org/cancer/managing-cancer/side-effects/hair-skin-nails/rashes-skin-changes.html **14.** American Cancer Society. What to do for peripheral neuropathy. Updated January 2026. Accessed February 11, 2026. https://www.cancer.org/content/dam/cancer-org/cancer-control/en/booklets-flyers/getting-help-for-peripheral-neuropathy.pdf **15.** American Cancer Society. Nutrition for the person getting cancer. Updated October 2024. Accessed February 11, 2026. https://www.cancer.org/content/dam/cancer-org/cancer-control/en/booklets-flyers/nutrition-for-the-patient-with-cancer-during-treatment.pdf **16.** American Cancer Society. Preventing infections in people with cancer. Updated December 4, 2025. Accessed February 12, 2026. https://www.cancer.org/cancer/managing-cancer/side-effects/infections/preventing-infections-in-people-with-cancer.html **17.** American Cancer Society. Fevers. Updated February 13, 2024. Accessed February 12, 2026. https://www.cancer.org/cancer/managing-cancer/side-effects/infections/fever.html

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

astellas Pfizer Oncology

© 2026 Astellas Pharma Inc. or its affiliates and Pfizer Inc.
All rights reserved. MAT-US-PAD-2026-00964 09/26
All trademarks are the property of their respective owners.

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