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

SUPPORT SOLUTIONS℠

PADCEVSupportSolutions.com
1-888-402-0627
1-877-747-6843 (fax)
Monday–Friday, 8:30 AM–8:00 PM ET

Coding and Billing Guide

for PADCEV® (enfortumab vedotin-ejfv)

BOXED WARNING: SERIOUS SKIN REACTIONS

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

Indication

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

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

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

PLEASE SEE IMPORTANT SAFETY INFORMATION ON PAGES 18-23.
PLEASE CLICK HERE FOR FULL PRESCRIBING INFORMATION, INCLUDING BOXED WARNING.

Table of Contents

Introduction

Accurate and appropriate coding and billing can help avoid delays in claims processing and facilitate timely reimbursement. Astellas and Pfizer are providing this guide as an educational reference, providing general coding and billing information to facilitate medically appropriate patient access to PADCEV® (enfortumab vedotin-ejfv).

Because insurance coverage, coding, claims filing, and reimbursement vary by setting of care and payer type, the information included in this guide is general. Additional information may exist, and actual coverage and reimbursement decisions are made by individual payers. Healthcare providers should always contact the applicable third-party payer for specific information on coding and billing requirements prior to initiating therapy.

This guide and the information contained herein is offered for informational purposes only and is not intended to provide reimbursement or legal advice. While Astellas and Pfizer have made every effort to be current as of the publication date of this guide, the information may not be current when you view it. Each healthcare provider is responsible for determining the appropriate codes, coverage, and payment for individual patients. Astellas and Pfizer do not guarantee third-party coverage or payment or reimbursement for claims.

Minimizing Claim Delays and Denials: Key Considerations

Claim processing delays and denials may result from:

- Missing, invalid, or mismatched coding (e.g., CPT®, HCPCS, ICD-10-CM)
- Missing or incorrect National Drug Code (NDC)
- Inaccurate patient or provider information
- Missing prior authorization documentation (e.g., prior authorization number)
- Non-compliance with payer-specific submission protocols

By providing complete and accurate information and following relevant submission protocols, providers can enhance claim processing efficiency.

Reminders Before Submitting Claims

The following reminders may help when submitting claims for PADCEV:

- Determine if PADCEV is covered as a medical or pharmacy benefit prior to infusion and if there are any applicable prior authorization requirements
- Accurately complete and submit the prior authorization form, if required
- Ensure medical records include full and proper documentation of the patient's history, prior therapy, and rationale for treatment to justify coding
- Specify the correct number of billing units on the CMS-1500 Claim Form or on the UB-04/CMS-1450 Claim Form. Dosing for PADCEV is weight based. Therefore, ensure the actual dose administered to the patient is reflected in the billing units (see pages 10 and 12 for instructions on filling out claim forms)
- If required, include a Letter of Medical Necessity that provides the patient's medical history and rationale for the therapy
- Verify that all identification numbers and names are entered correctly
- Use the correct ICD-10-CM, CPT®, and HCPCS codes, including modifiers if applicable
- Verify the proper use of billing codes
- For the hospital outpatient setting, confirm that the correct revenue code is used with the appropriate supporting HCPCS code
- Submit the claim in a timely fashion
- Track clearinghouse claims to ensure successful transmission

If you have questions or need assistance with benefits investigation, prior authorization, denial appeals, or coding and billing for PADCEV, please visit **PADCEVSupportSolutions.com** or call PADCEV Support Solutions at 1-888-402-0627, Monday–Friday, 8:30 AM–8:00 PM ET.

IMPORTANT INFORMATION: The coding, coverage, and payment information contained herein is gathered from various resources, general in nature, and subject to change without notice. Third-party payment for medical products and services is affected by numerous factors. It is always the provider's responsibility to determine the appropriate healthcare setting and to submit true and correct claims conforming to the requirements of the relevant payer for those products and services rendered. Pharmacies (or any other provider submitting a claim) should contact third-party payers for specific information on their coding, coverage, and payment policies. Information and materials provided by PADCEV Support Solutions are to assist providers, but the responsibility to determine coverage, reimbursement, and appropriate coding for a particular patient and/or procedure remains at all times with the provider and information provided by PADCEV Support Solutions, Astellas, or Pfizer should in no way be considered a guarantee of coverage or reimbursement for any product or service.

Relevant Billing Codes for PADCEV® (enfortumab vedotin-ejfv)

International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes

ICD-10-CM codes are used to identify a patient's diagnosis. At least one ICD-10-CM diagnosis code must be included in all hospital and physician office claims to describe the patient's condition.

Select Malignant Neoplasms of Urinary Tract[1] ICD-10-CM Codes	Code Description
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C66.1	Malignant neoplasm of right ureter
C66.2	Malignant neoplasm of left ureter
C66.9	Malignant neoplasm of unspecified ureter
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
C68.0	Malignant neoplasm of urethra
C68.8	Malignant neoplasm of overlapping sites of urinary organs

The ICD-10-CM diagnosis codes listed above are provided only as examples of potentially relevant codes. Providers should consult a current ICD-10-CM manual and select the most appropriate diagnosis code(s) to accurately describe a patient's condition. All diagnosis codes should be supported with adequate documentation.

The Healthcare Common Procedure Coding System (HCPCS) codes are listed below and the billing codes are on the next page.

It is the healthcare provider's responsibility to determine the appropriate codes and to submit accurate claims for products and services provided. Astellas and Pfizer do not guarantee coverage and/or reimbursement for PADCEV. Coverage, coding, and reimbursement policies vary significantly by payer, patient, and setting of care. Actual coverage and reimbursement decisions are made by individual payers following the receipt of claims. Healthcare providers should verify coverage, coding, and reimbursement guidelines on a case-by-case basis.

Healthcare Common Procedure Coding System

The HCPCS is used to identify products, supplies, and services that are billed to private and government payers by hospitals, physicians, and other healthcare professionals.

HCPCS Code[2]	Description	Billing Unit	Payers and Settings of Care[3]
J9177	Injection, enfortumab vedotin-ejfv, 0.25 mg	0.25 mg = 1 billing unit	Most payers (eg, commercial, Medicare, and Medicaid) and care settings (eg, hospital outpatient and physician office)

One billing unit of J9177 equals 0.25 mg of enfortumab vedotin-ejfv. As a result, 80 units equals 1 single-dose 20-mg vial and 120 units equals 1 single-dose 30-mg vial. Actual units reported will vary by dosage required for each individual patient.

This guide is offered for informational purposes only and is not intended to provide reimbursement or legal advice. Each healthcare provider is responsible for determining the appropriate codes, coverage, and payment for individual patients. Astellas and Pfizer do not guarantee third-party coverage or payment or reimbursement for denied claims.

Relevant Billing Codes for PADCEV® (enfortumab vedotin-ejfv)

Modifier Codes (JW, JZ, TB)

Payers such as Medicare may require the use of specific modifiers, including those used to denote acquisition of a drug or biological under the 340B Drug Pricing Program. The requirement and appropriate utilization of each modifier should be confirmed with the payer.

Code[4,5]	Description
JW	Discarded drug not administered (drug amount discarded/not administered to any patient)
JZ	Zero drug wasted (zero drug amount discarded/not administered to any patient)
TB	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes

Medicare requires providers and suppliers to report the JW modifier on Part B drug claims for a separately payable drug with unused and discarded amounts from single-dose containers or single-use packages of such drug. Also, providers and suppliers must document the amount of discarded drugs or biologicals in Medicare beneficiaries' medical records. Note: Either the JW or JZ modifier must be reported, for a given single-dose container/single-use package, but not both.[4]

Starting January 1, 2025, the Centers for Medicare & Medicaid Services is requiring all 340B-covered entities to report the TB modifier on claims for separately payable drugs acquired through the 340B Program. The JG modifier has been discontinued and replaced with the TB modifier.[5]

National Drug Code (NDC)

You may be required to include an NDC for PADCEV on a claim form. The 11-digit NDCs are listed below.

NDC for PADCEV[6]	Description
51144-0020-01	20 mg lyophilized powder in a single-dose vial for reconstitution
51144-0030-01	30 mg lyophilized powder in a single-dose vial for reconstitution

Note that the product's NDC has been "zero-filled" to ensure creation of an 11-digit code that meets Health Insurance Portability and Accountability Act (HIPAA) standards.[7] The 11-digit NDC is to be preceded by the qualifier "N4" for payers that require it. This is typically followed by the quantity qualifier and the quantity administered.[8]

Current Procedural Terminology® (CPT®) Codes for Drug Administration Service

The appropriate CPT® code for the administration of PADCEV will depend on the actual service performed.

CPT®[a] Code[9]	Description
96413	Chemotherapy administration, intravenous infusion technique, up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique, each additional hour (list separately in addition to code for primary procedure)

Healthcare providers should consult the current CPT® manual and always select the code that accurately describes the administration service performed for the patient. Healthcare providers should also contact the payer for additional coding information required.

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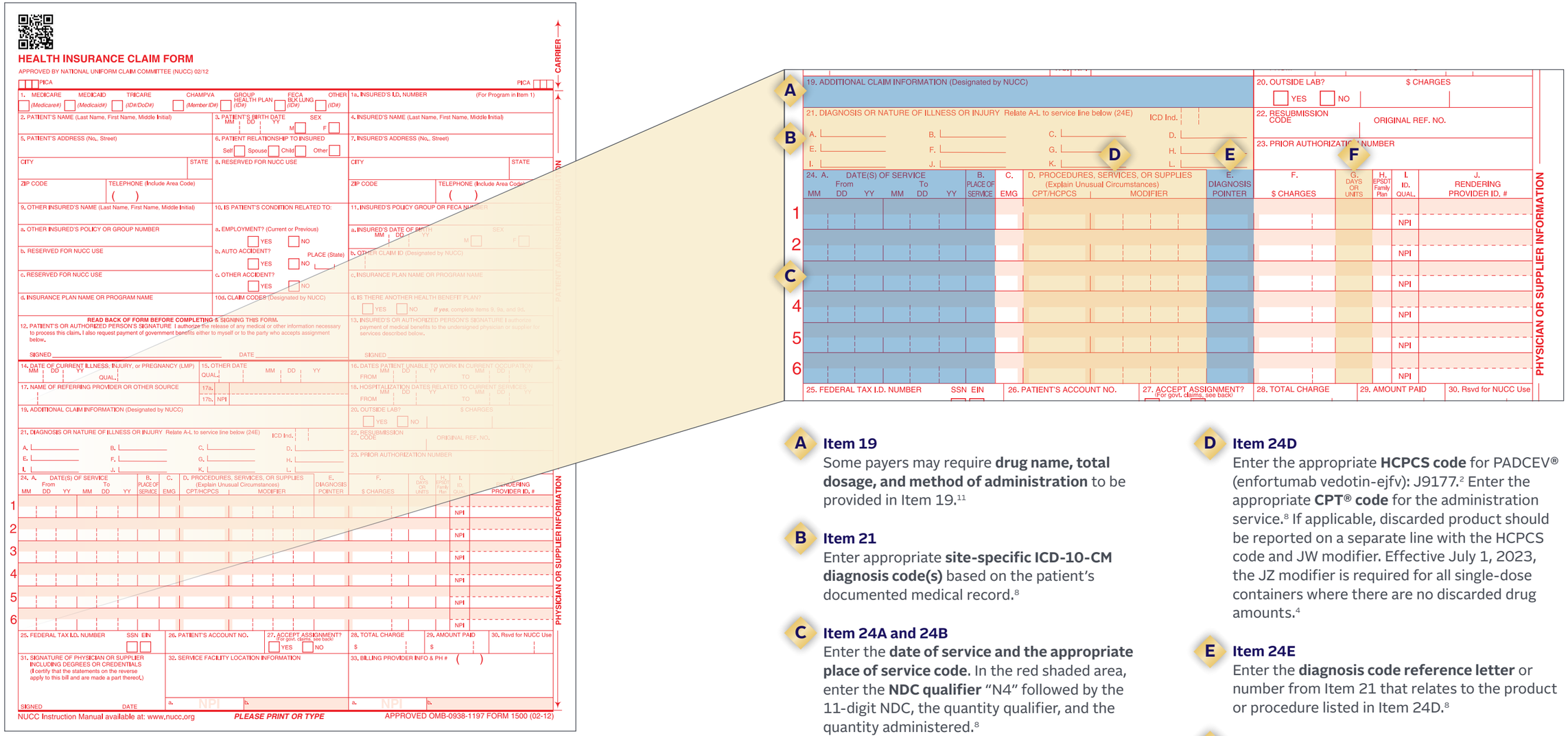
Sample Claim Form

Physician Office CMS-1500 Claim Form[10]



HEALTH INSURANCE CLAIM FORM

APPROVED BY NATIONAL UNIFORM CLAIM COMMITTEE (NUCC) 02/12

PICA

1. MEDICARE (Medicare#) MEDICAID (Medicaid#) TRICARE (ID#/DoD#) CHAMPVA (Member ID#) GROUP HEALTH PLAN (ID#) FECA BLK LUNG (ID#) OTHER (ID#)

1a. INSURED'S I.D. NUMBER (For Program in Item 1)

2. PATIENT'S NAME (Last Name, First Name, Middle Initial)

3. PATIENT'S BIRTH DATE MM DD YY SEX M F

4. INSURED'S NAME (Last Name, First Name, Middle Initial)

5. PATIENT'S ADDRESS (No., Street)

6. PATIENT RELATIONSHIP TO INSURED Self Spouse Child Other

7. INSURED'S ADDRESS (No., Street)

CITY STATE

8. RESERVED FOR NUCC USE

CITY STATE

ZIP CODE TELEPHONE (Include Area Code) ( )

ZIP CODE TELEPHONE (Include Area Code) ( )

9. OTHER INSURED'S NAME (Last Name, First Name, Middle Initial)

10. IS PATIENT'S CONDITION RELATED TO:

11. INSURED'S POLICY GROUP OR FECA NUMBER

a. OTHER INSURED'S POLICY OR GROUP NUMBER

a. EMPLOYMENT? (Current or Previous) YES NO

a. INSURED'S DATE OF BIRTH MM DD YY SEX M F

b. RESERVED FOR NUCC USE

b. AUTO ACCIDENT? YES NO PLACE (State)

b. OTHER CLAIM ID (Designated by NUCC)

c. RESERVED FOR NUCC USE

c. OTHER ACCIDENT? YES NO

c. INSURANCE PLAN NAME OR PROGRAM NAME

d. INSURANCE PLAN NAME OR PROGRAM NAME

10d. CLAIM CODES (Designated by NUCC)

d. IS THERE ANOTHER HEALTH BENEFIT PLAN? YES NO If yes, complete items 9, 9a, and 9d.

READ BACK OF FORM BEFORE COMPLETING & SIGNING THIS FORM.

12. PATIENT'S OR AUTHORIZED PERSON'S SIGNATURE I authorize the release of any medical or other information necessary to process this claim. I also request payment of government benefits either to myself or to the party who accepts assignment below.

SIGNED DATE

13. INSURED'S OR AUTHORIZED PERSON'S SIGNATURE I authorize payment of medical benefits to the undersigned physician or supplier for services described below.

SIGNED

14. DATE OF CURRENT ILLNESS, INJURY, or PREGNANCY (LMP) MM DD YY QUAL.

15. OTHER DATE QUAL. MM DD YY

16. DATES PATIENT UNABLE TO WORK IN CURRENT OCCUPATION MM DD YY FROM MM DD YY TO

17. NAME OF REFERRING PROVIDER OR OTHER SOURCE

17a.

17b. NPI

18. HOSPITALIZATION DATES RELATED TO CURRENT SERVICES MM DD YY FROM MM DD YY TO

19. ADDITIONAL CLAIM INFORMATION (Designated by NUCC)

20. OUTSIDE LAB? YES NO $ CHARGES

21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY Relate A-L to service line below (24E) ICD Ind.

A. B. C. D. E. F. G. H. I. J. K. L.

22. RESUBMISSION CODE ORIGINAL REF. NO.

23. PRIOR AUTHORIZATION NUMBER

24. A. DATE(S) OF SERVICE From MM DD YY	To MM DD YY	B. PLACE OF SERVICE	C. EMG	D. PROCEDURES, SERVICES, OR SUPPLIES (Explain Unusual Circumstances) CPT/HCPCS	MODIFIER	E. DIAGNOSIS POINTER	F. $ CHARGES	G. DAYS OR UNITS	H. EPSDT Family Plan	I. ID. QUAL.	J. RENDERING PROVIDER ID. #
1										NPI	
2										NPI	
3										NPI	
4										NPI	
5										NPI	
6										NPI	

25. FEDERAL TAX I.D. NUMBER SSN EIN

26. PATIENT'S ACCOUNT NO.

27. ACCEPT ASSIGNMENT? (For govt. claims, see back) YES NO

28. TOTAL CHARGE $

29. AMOUNT PAID $

30. Rsvd for NUCC Use

31. SIGNATURE OF PHYSICIAN OR SUPPLIER INCLUDING DEGREES OR CREDENTIALS (I certify that the statements on the reverse apply to this bill and are made a part thereof.)

SIGNED DATE

32. SERVICE FACILITY LOCATION INFORMATION

a. NPI b.

33. BILLING PROVIDER INFO & PH # ( )

a. NPI b.

NUCC Instruction Manual available at: www.nucc.org **PLEASE PRINT OR TYPE** APPROVED OMB-0938-1197 FORM 1500 (02-12)

CARRIER

PATIENT AND INSURED INFORMATION

PHYSICIAN OR SUPPLIER INFORMATION

This sample form is provided for informational purposes only. The accurate completion of claims documentation is the responsibility of the healthcare provider. Astellas and Pfizer do not guarantee reimbursement for any services or product.

A **Item 19**
Some payers may require **drug name, total dosage, and method of administration** to be provided in Item 19.[11]

B **Item 21**
Enter appropriate **site-specific ICD-10-CM diagnosis code(s)** based on the patient's documented medical record.[8]

C **Item 24A and 24B**
Enter the **date of service and the appropriate place of service code**. In the red shaded area, enter the **NDC qualifier** "N4" followed by the 11-digit NDC, the quantity qualifier, and the quantity administered.[8]

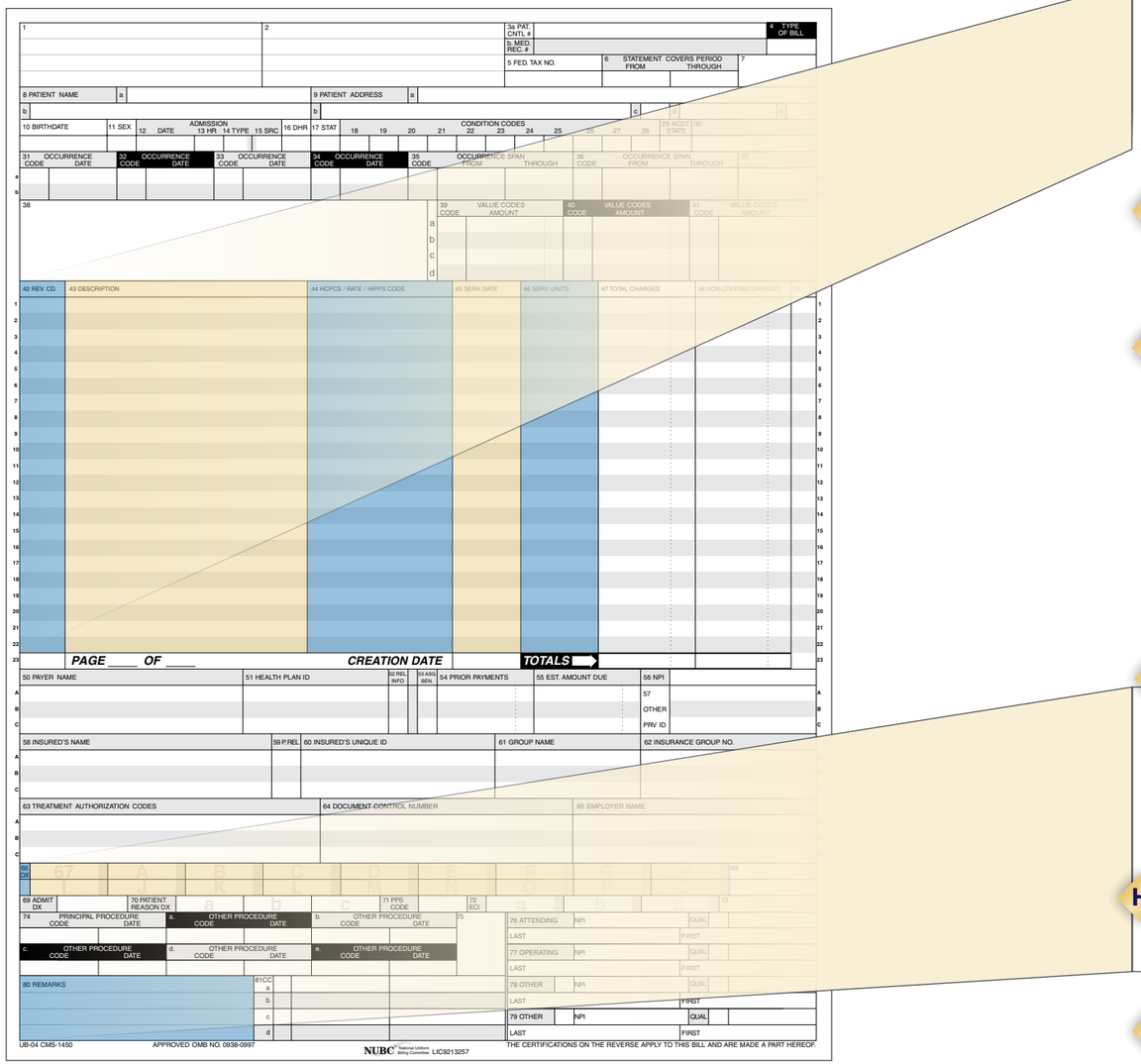
D **Item 24D**
Enter the appropriate **HCPCS code** for PADCEV® (enfortumab vedotin-ejfv): J9177.[2] Enter the appropriate **CPT® code** for the administration service.[8] If applicable, discarded product should be reported on a separate line with the HCPCS code and JW modifier. Effective July 1, 2023, the JZ modifier is required for all single-dose containers where there are no discarded drug amounts.[4]

E **Item 24E**
Enter the **diagnosis code reference letter** or number from Item 21 that relates to the product or procedure listed in Item 24D.[8]

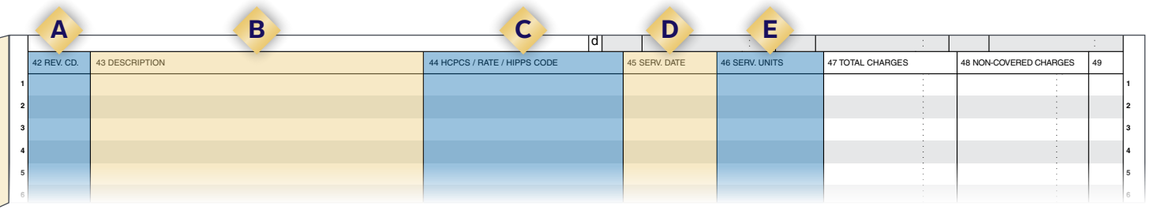
F **Item 24G**
Report **billing units** here. 0.25 mg = 1 billing unit. Actual units reported will vary by dosage required for each individual patient.[2,8]

Sample Claim Form

Outpatient Hospital CMS-1450 (UB-04) Claim Form[12]



This sample form is provided for informational purposes only. The accurate completion of claims documentation is the responsibility of the healthcare provider. Astellas and Pfizer do not guarantee reimbursement for any services or product.



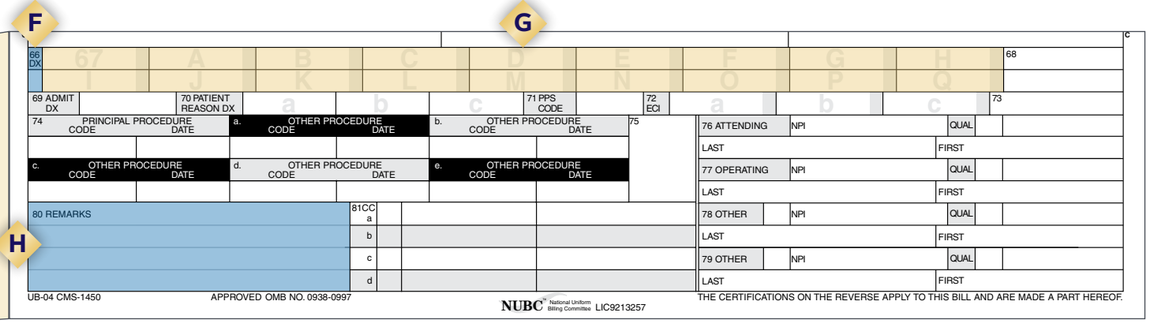
A **Item 42**
Enter a 4-digit **revenue code** that best describes the service provided, in accordance with the hospital billing policy.[13]

B **Item 43**
Enter the corresponding description for the revenue code listed in Item 42. When required, enter the **NDC qualifier** "N4" followed by the 11-digit NDC, the quantity qualifier, and the quantity administered.[13]

C **Item 44**
Enter the appropriate **HCPCS code** for PADCEV® (enfortumab vedotin-ejfv): J9177.[2,13] If applicable, discarded product should be reported on a separate line with the HCPCS code and JW modifier. Effective July 1, 2023, the JZ modifier is required for all single-dose containers where there are no discarded drug amounts.[4]

D **Item 45**
Enter the **date of service.**[13]

E **Item 46**
Report **billing units** here. 0.25 mg = 1 billing unit. Actual units reported will vary by dosage required for each individual patient.[2,13]



F **Item 66**
Enter the appropriate **diagnosis code qualifier.**[13]

G **Item 67A-67Q**
Enter the **site-specific ICD-10-CM diagnosis codes** for the malignancy being treated as documented in the patient's medical records. Other diagnosis codes are required when other conditions coexist or develop during the patient's treatment.[13]

H **Item 80**
Some payers may require additional information, such as the **date the drug was furnished to the beneficiary** and 11-digit NDC, to be entered in Item 80. Requirements vary by payer.[13,14]

PLEASE SEE IMPORTANT SAFETY INFORMATION ON PAGES 18-23.
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PADCEV® enfortumab vedotin-ejfv Injection for IV infusion 20 mg & 30 mg vials
SUPPORT SOLUTIONS℠

Claims Submission Checklist

A Summary of Key Information to Consider for Submitting Claims for PADCEV® (enfortumab vedotin-ejfv)

Use appropriate codes to report the patient's condition, the drugs the patient received, and the services provided[a]:

- ☐ **ICD-10-CM code** (refer to page 6)
- ☐ **J-code** (refer to page 7)
- ☐ **CPT® code** (refer to page 9)
- ☐ **Relevant modifiers, as necessary (JW or JZ)** (refer to page 8)

Include additional information requested by the payer

- ☐ **Product name**
- ☐ **Dosage**
- ☐ **NDC**
  - Carton of **one 20 mg single-dose vial** (NDC 51144-020-01)
  - Carton of **one 30 mg single-dose vial** (NDC 51144-030-01)
- ☐ **Route of administration**
- ☐ **Unit description**

[a]It is always the provider's responsibility to determine the appropriate healthcare setting and to submit true and correct claims conforming to the requirements of the relevant payer for those products and services rendered. The responsibility to determine coverage, reimbursement, and appropriate coding for a particular patient and/or procedure remains at all times with the provider.

Additional Information

A Summary of Key Information to Consider for Submitting Claims for PADCEV

Attach additional information to the claim if necessary:

- ☐ **Letter of medical necessity**
- ☐ **Prescribing Information**
- ☐ **Patient notes**

- ☐ Review claim for accuracy, including patient identification numbers, coding, and number of units
- ☐ File claim as soon as possible and within payer filing time requirements
- ☐ Reconcile claim reports promptly and thoroughly to ensure claims have been appropriately processed and paid
- ☐ Verify that payment amounts correspond with your public payer allowables and your private payer contracts

PADCEV Support Solutions℠

PADCEV Support Solutions offers access and reimbursement support to help patients access PADCEV® (enfortumab vedotin-ejfv). PADCEV Support Solutions provides information regarding patient health coverage, financial assistance information that may be available to help patients with financial needs, and coding and billing information for PADCEV.

Coverage Support

- Benefits investigation
- Prior authorization assistance
- Appeals assistance

Coding and Billing

- Coding and billing information
- Appeals information

Patient Assistance

- Copay Assistance Program[a]
- Patient Assistance Program[a]
- Financial assistance information

Patient Support

- Patient Connect

[a]Program is subject to eligibility restrictions and Program terms and conditions.

References

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Indication and Important Safety Information

BOXED WARNING: SERIOUS SKIN REACTIONS

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

Indication

PADCEV, in combination with pembrolizumab, 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.

Important Safety Information

Warnings and Precautions

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

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

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

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 DKA occurred in one patient each (0.1%). The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher body mass index and in patients with higher baseline A1C. The median time to onset of hyperglycemia was 0.5 months (range: 0 to 20 months). Hyperglycemia led to discontinuation of PADCEV in 0.7% of patients. Five percent (5%) of patients required initiation of insulin therapy for treatment of hyperglycemia. Of the patients who initiated insulin therapy for treatment of hyperglycemia, 66% (23/35) discontinued insulin at the time of last evaluation. Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia. If blood glucose is elevated (>250 mg/dL), withhold PADCEV.

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

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

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Important Safety Information (continued)

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® (enfortumab vedotin-ejfv) for patients who develop Grade 2 pneumonitis/ILD and consider dose reduction. Permanently discontinue PADCEV in all patients with Grade 3 or 4 pneumonitis/ILD.

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

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

Monitor patients for symptoms of new or worsening PN and consider dose interruption or dose reduction of PADCEV when PN occurs. Permanently discontinue PADCEV in patients who develop Grade ≥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 pembrolizumab)

Increased aspartate aminotransferase (AST), increased creatinine, rash, increased glucose, PN, increased lipase, decreased lymphocytes, increased alanine aminotransferase (ALT), decreased hemoglobin, fatigue, decreased sodium, decreased phosphate, decreased albumin, pruritus, diarrhea, alopecia, decreased weight, decreased appetite, increased urate, decreased neutrophils, decreased potassium, dry eye, nausea, constipation, increased potassium, dysgeusia, urinary tract infection and decreased platelets.

Most common adverse reactions, including laboratory abnormalities (≥20%) (PADCEV monotherapy)

Increased glucose, increased AST, decreased lymphocytes, increased creatinine, rash, fatigue, PN, decreased albumin, decreased hemoglobin, alopecia, decreased appetite, decreased neutrophils, decreased sodium, increased ALT, decreased phosphate, diarrhea, nausea, pruritus, increased urate, dry eye, dysgeusia, constipation, increased lipase, decreased weight, decreased platelets, abdominal pain, dry skin.

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

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

Adverse reactions leading to discontinuation of PADCEV occurred in 35% of patients. The **most common adverse reactions (≥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%).

Important Safety Information (continued)

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

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

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

Serious adverse reactions occurred in 47% of patients treated with PADCEV; the most common (≥2%) were urinary tract infection, acute kidney injury (7% each), and pneumonia (5%). **Fatal adverse reactions** occurred in 3% of patients, including multiorgan dysfunction (1%), hepatic dysfunction, septic shock, hyperglycemia, pneumonitis/ILD, and pelvic abscess (0.3% each). **Adverse reactions leading to discontinuation** occurred in 17% of patients; the most common (≥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, and fatigue (3% each).

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

Serious adverse reactions occurred in 39% of patients treated with PADCEV; the most common (≥3%) were pneumonia, sepsis, and diarrhea (5% each). **Fatal adverse reactions** occurred in 8% of patients, including acute kidney injury (2.2%), metabolic acidosis, sepsis, multiorgan dysfunction, pneumonia, and pneumonitis/ILD (1.1% each). **Adverse reactions leading to discontinuation** occurred in 20% of patients; the most common (≥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, and hyperglycemia (3% each). **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.

Contact PADCEV Support Solutions℠

There are 3 ways to contact PADCEV Support Solutions for assistance:

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