

## Clinical Policy: Enfortumab Vedotin-ejfv (Padcev)

Reference Number: PA.CP.PHAR.455

Effective Date: 10/2020

Last Review Date: 01/2025

### Description

Enfortumab vedotin-ejfv (Padcev™) is a Nectin-4-directed antibody and microtubule inhibitor conjugate.

### FDA Approved Indication(s)

Padcev is indicated:

- In combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph, as neoadjuvant treatment and then continued after cystectomy as adjuvant treatment, for the treatment of adult patients with muscle invasive bladder cancer (MIBC) who are ineligible for cisplatin-containing chemotherapy
- In combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC).
- As a single agent 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 a platinum-containing chemotherapy
  - are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of PA Health & Wellness® that Padcev is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Bladder Cancer (must meet all):

1. Diagnosis of urothelial carcinoma or MIBC;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age  $\geq$  18 years;
4. For MIBC: Both of the following (a and b):
  - a. Prescribed in one of the following ways (i or ii):
    - i. Neoadjuvant treatment in combination with Keytruda® or Keytruda Qlex™ for up to 3 cycles;
    - ii. Adjuvant treatment in combination Keytruda or Keytruda Qlex following neoadjuvant treatment and cystectomy for up to 6 cycles;
  - b. Member is ineligible for cisplatin-containing chemotherapy;
5. For recurrent, locally advanced or metastatic urothelial carcinoma, one of the following (a or b):
  - a. Prescribed as a single agent, and one of the following (i or ii):

- i. Failure of both of the following (1 and 2):
  1. Platinum-containing chemotherapy (*see Appendix B*);
  2. PD-1 or PD-L1 inhibitor (*see Appendix B*);
- ii. Member is ineligible for cisplatin-containing chemotherapy and has previously received one or more prior lines of therapy (*see Appendix B*);
- b. Prescribed in combination with Keytruda® or Keytruda Qlex;
6. Request meets one of the following (a, b or c):
  - a. If prescribed as a single agent: Dose does not exceed 125 mg on Days 1, 8, and 15 of a 28-day cycle;
  - b. If prescribed in combination with Keytruda or Keytruda Qlex: Dose does not exceed 1.25 mg/kg (up to 125 mg) on days 1 and 8 of a 21-day cycle;
  - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 12 months**

**B. Other diagnoses/indications**

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**II. Continued Therapy**

**A. Bladder Cancer (must meet all):**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. If request is for MIBC, maximum duration of therapy does not exceed both of the following (a and b):
  - a. For neoadjuvant treatment: 3 cycles;
  - b. For adjuvant treatment: 6 cycles;
4. If request is for a dose increase, request meets one of the following (a, b or c):
  - a. For urothelial carcinoma if prescribed as a single agent: New dose does not exceed 125 mg on Days 1, 8 and 15 of a 28-day cycle;
  - b. If prescribed in combination with Keytruda or Keytruda Qlex: New dose does not exceed 1.25 mg/kg (up to 125 mg) on days 1 and 8 of a 21-day cycle;
  - c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 12 months**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration

PD-1: programmed death receptor-1

PD-L1: programmed death-ligand

MIBC: muscle invasive bladder cancer

mUC: metastatic urothelial cancer

NCCN: National Comprehensive Cancer Network

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<b>Examples of platinum-containing regimens</b>		
DDMVAC (dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin)	Varies	Varies
gemcitabine with either cisplatin or carboplatin	Varies	Varies
<b>Examples of PD-1 inhibitors</b>		
Keytruda <sup>®</sup> (pembrolizumab)	Varies	Varies
Keytruda Qlex <sup>™</sup> (pembrolizumab and berahyaluronidase alfa-pmp)	Varies	Varies
Opdivo <sup>®</sup> (nivolumab)	Varies	Varies
Opdivo Qvantig <sup>™</sup> (nivolumab and hyaluronidase-nvhy)	Varies	Varies
<b>Examples of PD-L1 inhibitors</b>		
Tecentriq <sup>®</sup> (atezolizumab)	Varies	Varies
Imfinzi <sup>®</sup> (durvalumab)	10 mg/kg IV infusion every 2 weeks	Varies
Bavencio <sup>®</sup> (avelumab)	800 mg IV infusion once every 2 weeks	Varies
<b>Other recommended regimens</b>		
gemcitabine	Varies	Varies
gemcitabine and paclitaxel	Varies	Varies
ifosfamide, doxorubicin, gemcitabine	Varies	Varies

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

Contraindication(s): None reported

Boxed warning(s): Serious skin reactions

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
MIBC	1.25 mg/kg (up to a maximum dose of 125 mg) given as an IV infusion over 30 minutes as neoadjuvant treatment on Days 1 and 8 of each 21-day cycle for 3 cycles or until disease progression that precludes curative intent cystectomy or unacceptable toxicity, followed by adjuvant treatment on Days 1 and 8 of each 21-day cycle for 6 cycles or until disease recurrence or unacceptable toxicity	1.25 mg/kg (up to a maximum dose of 125 mg)
Urothelial cancer	<i>As a single agent:</i> 1.25 mg/kg (up to a maximum dose of 125 mg) given as an intravenous infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity  <i>In combination with Keytruda:</i> 1.25 mg/kg (up to a maximum dose of 125 mg) given as an IV infusion over 30 minutes on Days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity	1.25 mg/kg (up to a maximum dose of 125 mg)

**VI. Product Availability**

Single-dose vial for injection: 20 mg, 30 mg

**VII. References**

1. Padcev Prescribing Information. Northbrook, IL: Astellas Pharma US, Inc; November 2025. Available at: <https://www.padcev.com>. Accessed November 25, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed November 19, 2025.
3. National Comprehensive Cancer Network. Bladder Cancer Version 2.2025. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/bladder.pdf](https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf). Accessed November 19, 2025.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 19, 2025.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9177	Injection, enfortumab vedotin-ejfv, 0.25mg

Reviews, Revisions, and Approvals	Date
Policy created.	10/2020
1Q 2021 annual review: recurrent UC added and trial settings (e.g., neoadjuvant) removed to encompass NCCN recommended uses; references reviewed and updated.	01/2021
1Q 2022 annual review: updated HCPCS codes for Padcev and Appendix C with new boxed warning; references reviewed and updated.	01/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
RT4: added additional urothelial cancer indication in combination with pembrolizumab for patients ineligible for cisplatin-containing chemotherapy; added urologist prescriber per previously P&T approved approach for urological cancers.	05/2023
1Q 2024 annual review: removed for patients ineligible for cisplatin-containing chemotherapy due to FDA updated language; references reviewed and updated.	01/2024
1Q 2025 annual review: no significant changes; references reviewed and updated.	01/2025
1Q 2026 annual review: extended initial approval duration from 6 to 12 months for this maintenance medication for a chronic condition; added option to be prescribed in combination with Keytruda Qlex; references reviewed and updated. RT4: new indication for MIBC added per updated prescribing information.	01/2026