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:

- As a single agent for the treatment of adult patients with locally advanced or metastatic urothelial cancer 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
- In combination with pembrolizumab for the treatment of adult patients with locally advanced or metastatic urothelial cancer.

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. Urothelial Carcinoma (must meet all)**:**

1. Diagnosis of one of recurrent, locally advanced or metastatic (stage IV) urothelial carcinoma;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. 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 (s*ee Appendix B*);
         2. PD-1 or PD-L1 inhibitor (s*ee 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®;
5. 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: 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: 6 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. Urothelial Carcinoma (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 a dose increase, request meets one of the following (a, b or c):
   a. 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: 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
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
Examples of platinum-containing regimens		
DDMVAC (dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin)	Varies	Varies
gemcitabine with either cisplatin or carboplatin	Varies	Varies
Examples of PD-1 inhibitors		
Keytruda® (pembrolizumab)	Varies	Varies
Opdivo® (nivolumab)	Varies	Varies
Examples of PD-L1 inhibitors		
Tecentriq® (atezolizumab)	Varies	Varies
Imfinzi® (durvalumab)	10 mg/kg IV infusion every 2 weeks	Varies
Bavencio® (avelumab)	800 mg IV infusion once every 2 weeks	Varies
Other recommended regimens		
gemcitabine	Varies	Varies
gemcitabine and paclitaxel	Varies	Varies
ifosfamide, doxorubicin, gemcitabine	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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
Urothelial cancer	*As a single agent*: 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 *In combination with Keytruda*: 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	See dosing regimen

VI. Product Availability

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

VII. References

1. Padcev Prescribing Information. Northbrook, IL: Astellas Pharma US, Inc; August 2024. Available at: https://www.padcev.com. Accessed October 21, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 7, 2024.
3. National Comprehensive Cancer Network. Bladder Cancer Version 5.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed November 7, 2024.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 7, 2024.

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