Clinical Policy: Enfortumab Vedotin-ejfv (Padcev)

Reference Number: CP.PHAR.455
Effective Date: 03.01.20
Last Review Date: 02.26
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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)
- In combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph for the treatment of adult patients with locally advanced or metastatic urothelial cancer (la/mUC)
- As a single agent for the treatment of adult patients with la/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, or
  - 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 health plans affiliated with Centene Corporation® that Padcev is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of la/mUC or MIBC;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. For MIBC: Prescribed in one of the following ways (a or b):
   a. Neoadjuvant treatment in combination with Keytruda® or Keytruda Qlex™ for up to 3 cycles (cisplatin-ineligible) or 4 cycles (cisplatin-eligible);
   b. Adjuvant treatment in combination with Keytruda or Keytruda Qlex following neoadjuvant treatment and cystectomy for up to 6 cycles (cisplatin-ineligible) or 5 cycles (cisplatin-eligible);
5. For recurrent, la/mUC: Prescribed in one of the following ways (a or b):

a. As a single agent, and member previously received one or more prior lines of therapy (s*ee Appendix B*);
b. In combination with Keytruda or Keytruda Qlex as first-line or second-line systemic therapy;

6. Request meets one of the following (a, b, or c):*
   a. For urothelial cancer if prescribed as a single agent: Dose does not exceed 1.25 mg/kg (up to 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Padcev for a covered indication and has received this medication for at least 28 days;
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 (cisplatin-ineligible) or 4 cycles (cisplatin-eligible);
   b. For adjuvant treatment: 6 cycles (cisplatin-ineligible) or 5 cycles (cisplatin-eligible);

4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. For urothelial cancer if prescribed as a single agent: New dose does not exceed 1.25 mg/kg (up to 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*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 – CP.CPA.190 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

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
la/mUC: locally advanced or 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 for all relevant lines of business 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
Keytruda Qlex™ (pembrolizumab and berahyaluronidase alfa-pmp)	Varies	Varies
Opdivo® (nivolumab)	Varies	Varies
Opdivo Qvantig™ (nivolumab and hyaluronidase-nvhy)	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

Appendix D: General Information

- Cisplatin ineligibility is defined as meeting at least one of the following criteria: Creatinine clearance of less than 60 mL/min, ECOG PS 2 or higher, Grade 2 or higher hearing loss, NYHA Class III or higher heart failure, or Grade 2 or higher peripheral neuropathy.

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 on Days 1 and 8 of each 21-day cycle for the following duration of therapy: • Neoadjuvant treatment: 3 cycles (for cisplatin-ineligible) or 4 cycles (for cisplatin-eligible) or until	1.25 mg/kg (up to a maximum dose of 125 mg)

Indication	Dosing Regimen	Maximum Dose
	disease progression that precludes curative intent cystectomy or unacceptable toxicity • Adjuvant treatment: 6 cycles (for cisplatin-ineligible) or 5 cycles (for cisplatin-eligible) or until disease recurrence or unacceptable toxicity	
Urothelial cancer	*As a single agent*: 1.25 mg/kg (up to a maximum dose of 125 mg) given as an IV 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 or Keytruda Qlex*: 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 vials for injection: 20 mg, 30 mg

VII. References

1. Padcev Prescribing Information. Northbrook, IL: Astellas Pharma US, Inc; July 2026. Available at: https://www.padcev.com. Accessed July 14, 2026.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 16, 2026.
3. National Comprehensive Cancer Network. Bladder Cancer Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed July 14, 2026.
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, 0.25 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2022 annual review: no significant changes; updated HCPCS codes for Padcev and Appendix C with new boxed warning; references reviewed and updated.	10.18.21	02.22
Template changes applied to other diagnoses/indications.	09.28.22	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2023 annual review: no significant changes; references reviewed and updated.	11.10.22	02.23
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.	04.26.23	
Added Commercial line of business.	05.18.23	08.23
1Q 2024 annual review: no significant changes; references reviewed and updated. RT4: for urothelial cancer in combination with Keytruda, updated FDA-approved indication to full approval and removed requirement for cisplatin ineligibility per updated PI.	12.27.23	02.24
1Q 2025 annual review: no significant changes; references reviewed and updated.	10.21.24	02.25
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.	11.06.25	02.26
RT4: added new FDA-approved indication for MIBC in combination with Keytruda or Keytruda Qlex for neoadjuvant and adjuvant treatment (regardless of cisplatin eligibility); for la/mUC, revised to allow use as single agent after one or more prior of lines of therapy and clarified use should be first-line or second-line systemic therapy when prescribed in combination with Keytruda or Keytruda Qlex per NCCN.	07.14.26	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage

decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.