Clinical Policy: Enfortumab Vedotin-ejfv (Padcev)

Reference Number: CP.PHAR.455
Effective Date: 03.01.20
Last Review Date: 02.23
Line of Business: 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:

- 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, or
  - 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 who are not eligible for cisplatin-containing chemotherapy*

* This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

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

1. Diagnosis 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, b, or c):
   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 (s*ee Appendix B*);

b. Prescribed in combination with Keytruda®, and member is ineligible for cisplatin-containing chemotherapy;

5. Request meets one of the following (a, b, or c):*
   a. 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: 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: 6 months

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: 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: 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: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Urothelial Carcinoma (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 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 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: 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: 12 months

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: 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: 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: 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 – 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
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
Opdivo® (nivolumab)	Varies	Varies
Examples of PD-L1 inhibitors		
Tecentriq® (atezolizumab)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 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*: 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; April 2023. Available at: https://www.padcev.com. Accessed May 11, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 11, 2023.
3. National Comprehensive Cancer Network. Bladder Cancer Version 2.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed April 26, 2023.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed April 26, 2023.

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
Policy created.	01.14.20	02.20
1Q 2021 annual review: recurrent UC added and trial settings (e.g., neoadjuvant) removed to encompass NCCN recommended uses; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.10.20	02.21
RT4: added additional urothelial cancer indication in patients ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy	07.28.21	
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	
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	

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.