

Utilization Management and Clinical Medical Policy

Policy Name: Enfortumab vedotin-ejfv (Padcev®)	Policy Number: MP-RX-FP-70-23	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 11/30/2023	Effective Date: 7/1/2026
			Last Review Date: 7/1/2026	Frequently Revision: Annual

Service Category:

- | | |
|--|---|
| ☐ Anesthesia | ☐ Medicine Services and Procedures |
| ☐ Surgery | ☐ Evaluation and Management Services |
| ☐ Radiology Procedures | ☐ DME/Prosthetics or Supplies |
| ☐ Pathology and Laboratory Procedures | ☒ Other: Part B Drugs |

Service Description:

This document addresses the use of Enfortumab vedotin-ejfv (Padcev®), a Nectin-4-directed antibody and microtubule inhibitor conjugate approved by the Food and Drug Administration (FDA) for the treatment of certain patients with locally advanced or metastatic urothelial cancer.

Background Information:

The FDA approved indications for Padcev are for the treatment of adults 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 in those who are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy in the neoadjuvant/adjuvant, locally advanced, or metastatic setting. Padcev was approved under the FDA accelerated program based on tumor response rate. Continued approval is contingent upon confirmatory trials.

The FDA also approved Padcev in combination with Keytruda and Keytruda Qlex as neoadjuvant treatment and then continued after cystectomy as adjuvant treatment, for the treatment of muscle invasive bladder cancer (MIBC) who are ineligible for cisplatin-containing chemotherapy.

The National Comprehensive Cancer Network (NCCN) recommends Padcev as subsequent-line systemic therapy for locally advanced or metastatic urothelial cancer (1, 2A category) based on the same pivotal trial that helped to gain FDA approval. NCCN also provides 1, 2A recommendations for use as primary and subsequent treatment in muscle-invasive bladder cancer in combination with Keytruda and Keytruda Qlex.

Padcev has a black box warning for severe and fatal cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN).

Definitions and Measures

- Adjuvant therapy: Treatment given after the primary treatment to increase the chances of a cure; may include chemotherapy, radiation, hormone or biological therapy.
- Chemotherapy: Medical treatment of a disease, particularly cancer, with drugs or other chemicals. Disease Progression: Cancer that continues to grow or spread.
- ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:
 - 0 = Fully active, able to carry on all pre-disease performance without restriction

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- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light housework, office work
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
- 5 = Dead
- Immune checkpoint inhibitor: A type of drug that blocks certain proteins made by some types of immune system cells, such as T cells, and some cancer cells. When these proteins are blocked, the “brakes” on the immune system are released and T cells are able to kill cancer cells better. Examples of checkpoint proteins found on T cells or cancer cells include programmed death (PD)-1, PD-ligand 1 (PD-L1), and cytotoxic T-lymphocyte-associated antigen (CTLA)-4/B7-1/B7-2.
- Locally advanced cancer: Cancer that has spread only to nearby tissues or lymph nodes.
- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.
- Monoclonal antibody: A protein developed in the laboratory that can locate and bind to specific substances in the body and on the surface of cancer cells.
- Neoadjuvant therapy: Treatment given as a first step to shrink a tumor before the main treatment, which is usually surgery, is given. Examples of neoadjuvant therapy include chemotherapy, radiation therapy, and hormone therapy. It is a type of induction therapy.
- Programmed death (PD)-1 proteins: PD-1 proteins are found on T-cells and attach to PD ligands (PD-L1) found on normal (and cancer) cells (see immune checkpoint inhibitor above). Normally, this process keeps T-cells from attacking other cells in the body. However, this can also prevent T-cells from attacking cancer cells in the body. Examples of FDA approved anti-PD-1 agents include Keytruda (pembrolizumab), Opdivo (nivolumab), and Libtayo (cemiplimab).
- Programmed death ligand (PD-L)-1: The ligands found on normal (and cancer) cells to which the PD-1 proteins attach (see immune checkpoint inhibitor above). Cancer cells can have large amounts of PD-L1 on their surface, which helps them to avoid immune attacks. Examples of FDA approved anti-PD-L1 agents include Bavencio (avelumab), Tecentriq (atezolizumab), and Imfinzi (durvalumab).
- Urothelial carcinoma: A type of bladder cancer which occurs in the urinary tract system.

Approved Indications

- A. As a single agent for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC) who:
 - a. Have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum- containing chemotherapy, or

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- b. Are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.
- B. 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.
- C. In combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph, for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC).

Other Uses

- A. See background section above.

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Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Enfortumab vedotin-ejfv (Padcev®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.*)

Requests for Padcev (enfortumab vedotin-ejfv) may be approved if the following criteria are met (Label, NCCN 1, 2A):

- i. Individual has a diagnosis of recurrent locally advanced or metastatic urothelial cancer; **AND**
 - A. Individual is using in one of the following ways:
 1. In combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph as first-line systemic therapy; **OR**
 2. Individual is using as second line systemic therapy after:
 - a. Previous chemotherapy (no previous immunotherapy or enfortumab vedotin-ejfv); **OR**
 - b. Previous immunotherapy (no previous chemotherapy or enfortumab vedotin-ejfv); **AND**
 - c. Individual is using as a single agent or in combination with pembrolizumab; **OR**
 3. Individual is using as a single agent for subsequent therapy after progression in one of the following ways:
 - a. Anti-PD-1 or anti-PD-L1 agent and platinum-containing chemotherapy; **OR**
 - b. Individual is ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy;
 - ii. Individual has a diagnosis of muscle invasive bladder cancer (MIBC); **AND**
 - A. Individual is using in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph as either neoadjuvant or adjuvant treatment; **AND**
 - B. Individual is ineligible for cisplatin-containing chemotherapy.

B. Criteria For Continuation of Therapy

- i. MMM considers continuation of Enfortumab vedotin-ejfv (Padcev®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above

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(Criteria for Initial Approval) when there is no evidence of an unacceptable toxicity or disease progression while on the current regimen. The following information should be submitted for reauthorization:

- A. A current oncology note documenting the patient's response to treatment showing no progression of disease.
- B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

- i. Initial Approval Duration: Up to 6 months
- ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Padcev (enfortumab vedotin-ejfv) may not be approved for the following:

- i. Individuals with moderate or severe hepatic impairment (Child-Pugh B or C); **OR**
- ii. When the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

- i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Dosage Forms & Strengths	Indication	Recommended Dosing Regimen	Recommended Treatment Duration
Enfortumab vedotin-ejfv (Padcev®) for injection: 20 mg SDV 30 mg SDV	As a single agent for locally advanced or metastatic Urothelial Cancer (mUC)	1.25 mg/kg (up to a maximum of 125 mg for patients ≥ 100 kg) i.v. administered on Days 1, 8 and 15 of a 28-day cycle	Until disease progression or unacceptable toxicity.
	In combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmp for Neoadjuvant and Adjuvant (Muscle Invasive Bladder Cancer (MIBC))	1.25 mg/kg (up to a maximum of 125 mg for patients ≥ 100 kg) i.v. administered on Days 1 and 8 of a 21-day cycle	Neoadjuvant: 3 cycles or until disease progression that precludes curative intent cystectomy or unacceptable toxicity. Adjuvant: 6 cycles or until disease recurrence or unacceptable toxicity.
	In combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmp for locally advanced or metastatic Urothelial Cancer (mUC)		Until disease progression or unacceptable toxicity.
Exceptions			
None			

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
C61	Malignant neoplasm of prostate
C65.1-C65.9	Malignant neoplasm of renal pelvis
C66.1-C66.9	Malignant neoplasm of ureter
C67.0-C67.9	Malignant neoplasm of bladder
C68.0	Malignant neoplasm of urethra
C79.11-C79.19	Secondary malignant neoplasm of other urinary organs
Z92.21	Personal history of antineoplastic chemotherapy
Z92.22	Personal history of monoclonal drug therapy

HCPCS Codes:

Codes	Description
J9177	Injection, enfortumab vedotin-ejfv, 0.25 mg (Padcev)

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Reference Information:

1. Astellas Pharma US, Inc. (2025). PADCEV® (enfortumab vedotin-ejfv) for injection, for intravenous use: Prescribing information. Revised November 2025. Retrieved April 30, 2026, from https://astellas.us/docs/PADCEV_label.pdf
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2026. URL: <http://www.clinicalpharmacology.com>. Updated periodically.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. <http://dailymed.nlm.nih.gov/dailymed/about.cfm>.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2026; Updated periodically.
6. NCCN Clinical Practice Guidelines in Oncology™. © 2026 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>. Accessed on January 11, 2026.
 - a. Bladder Cancer. V3.2025. Revised December 19, 2025.
7. Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. N Engl J Med 2021; 384:1125-1135
8. Yu EY, Petrylak DP, O'Donnell PH, et al. Enfortumab vedotin after PD-1 or PD-L1 inhibitors in cisplatin-ineligible patients with advanced urothelial carcinoma (EV-201): a multicenter, single-arm, phase 2 trial. Lancet Oncol 2021; 22:872-882.

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Updated Background information to add a new FDA indication and NCCN recommendations. Updated Approved Indications and clinical criteria to add the FDA indication for use in muscle invasive bladder cancer in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph in those ineligible for cisplatin containing chemotherapy; and added “recurrent” disease state from NCCN recommendations. Coding Reviewed: Added ICD-10-CM C61, C67.0, and C68.0. Updated quantity limits table to include recommended dosage per indication and available dosage forms and strengths. Updated references and incorporated new policy template.	6/19/2026	7/1/2026
Annual Review	Added: C65.1-C65.9, C66.1-C66.9. Updated as NCCN category 1 use in combination with pembrolizumab as first-line systemic therapy. Added: per NCCN clinical guideline updates Bladder Cancer Version 1.2025: Individual is using as second line systemic therapy after: a. Previous chemotherapy (no previous immunotherapy or enfortumab vedotin-ejfv); OR b. Previous immunotherapy (no previous chemotherapy or enfortumab vedotin-ejfv); AND c. Individual is using as a single agent or in combination with pembrolizumab; (NCCN category 2A).	7/17/2025	8/8/2025
Annual Review	Update criteria with FDA label updates for use in combination with pembrolizumab. Remove ECOG requirements. Wording and formatting updates. Coding Reviewed: No changes.	11/18/2024	12/17/2024
Policy Inception	Elevance Health’s Medical Policy adoption.	N/A	11/30/2023