Padcev® (enfortumab vedotin-ejfv)
(Intravenous)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- 4680 billable units every 84 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Urothelial Carcinoma (Bladder Cancer) † ‡ [1-4,1e,3e,4e]

- Used in combination with pembrolizumab; **AND**
  - Used as first-line therapy; **AND**
  - Patient has one of the following diagnoses:
    - Locally advanced or metastatic urothelial carcinoma ‡
    - Metastatic primary carcinoma of the urethra ‡
    - Metastatic upper genitourinary (GU) tract tumors ‡
    - Metastatic urothelial carcinoma of the prostate ‡; **OR**
- Used as a single agent; **AND**
  - Patient has one of the following diagnoses:
    - Locally advanced or metastatic urothelial carcinoma †; **OR**
    - Muscle invasive bladder cancer with local recurrence or persistent disease in a preserved bladder treated with curative intent ‡; **OR**
    - Metastatic or local bladder cancer recurrence post-cystectomy treated with curative intent ‡; **OR**
    - Primary carcinoma of the urethra ‡; **AND**

- Used for recurrent *(excluding recurrence of stage T3-4 disease or palpable inguinal lymph nodes)* or metastatic disease; **OR**
- Metastatic upper genitourinary (GU) tract tumors ‡; **OR**
- Metastatic urothelial carcinoma of the prostate ‡; **AND**

- Used in one of the following treatment settings:
  - Patient was previously treated with platinum-containing chemotherapy* and checkpoint inhibitor therapy (if eligible); **OR**
  - Used as subsequent therapy in patients ineligible for cisplatin-containing chemotherapy***; OR**
  - Used as second-line therapy post-checkpoint inhibitor therapy for cisplatin ineligible patients

**** Note:*** [3,12,13]

- *Cisplatin-ineligible comorbidities may include the following: CrCl < 60 mL/min, PS ≥ 2, or KPS ≤ 70%, hearing loss of ≥ 25 decibels (dB) at two contiguous frequencies, grade ≥ 2 peripheral neuropathy, or NYHA Heart Failure class ≥ 3. Carboplatin may be substituted for cisplatin in the metastatic setting for cisplatin-ineligible patients such as those with a GFR less than 60 mL/min.*
- *Platinum-ineligible comorbidities may include the following: CrCl < 30 mL/min, ECOG PS ≥ 3, grade ≥ 2 peripheral neuropathy, or NYHA Heart Failure class > 3, etc.*

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hyperglycemia or diabetic ketoacidosis, severe pneumonitis/interstitial lung disease (ILD), severe peripheral neuropathy, ocular disorders including vision changes, severe skin reactions (e.g., Steven Johnson syndrome, toxic epidermal necrolysis, etc.), infusion site extravasation, etc.

V. Dosage/Administration [1]

Indication	Dose
Urothelial Carcinoma (Bladder Cancer)	**Single Agent** Administer 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) 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 Pembrolizumab** Administer 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) as an intravenous infusion over 30 minutes on Days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J9177 – Injection, enfortumab vedotin-ejfv, 0.25 mg: 1 billable unit = 0.25 mg

NDC(s):

- Padcev 20 mg single-dose vial: 51144-0020-xx
- Padcev 30 mg single-dose vial: 51144-0030-xx

VII. References (STANDARD)

1. Padcev [package insert]. Northbrook, IL; Astellas Pharma US, Inc; August 2024. Accessed February 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for enfortumab vedotin. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2025.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Bladder Cancer. Version 6.2024. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2025.
4. Rosenberg JE, O'Donnell PH, Balar AV, et al. Pivotal Trial of Enfortumab Vedotin in Urothelial Carcinoma After Platinum and Anti-Programmed Death 1/Programmed Death Ligand 1 Therapy. J Clin Oncol. 2019 Oct 10;37(29):2592-2600.

5. Gupta S, Sonpavde G, Grivas P, et al. Defining “platinum-ineligible” patients with metastatic urothelial cancer (mUC). J Clin Oncol. 2019 Mar 1;37(7_suppl):451.
6. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
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9. Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma. N Engl J Med. 2021 Mar 25;384(12):1125-1135. doi: 10.1056/NEJMoa2035807. Epub 2021 Feb 12.
10. Balar AV, McGregor BA, Rosenberg JE, et al. EV-201 Cohort 2: Enfortumab vedotin in cisplatin-ineligible patients with locally advanced or metastatic urothelial cancer who received prior PD-1/PD-L1 inhibitors. DOI: 10.1200/JCO.2021.39.6_suppl.394 Journal of Clinical Oncology 39, no. 6_suppl (February 20, 2021) 394-394.
11. Gupta S, Sonpavde G, Grivas P, et al. Defining “platinum-ineligible” patients with metastatic urothelial cancer (mUC). J Clin Oncol. 2019 Mar 1;37(7_suppl):451.
12. Gupta S, Bellmunt J, Plimack ER, et al. Defining “platinum-ineligible” patients with metastatic urothelial cancer (mUC). J Clin Oncol. 2022 June 1;40(16_suppl):4577.
13. Bellmunt, J. (2023). Treatment of metastatic urothelial cancer of the bladder and urinary tract. In Lerner SP, Shah S (Eds.), *UptoDate.* Last updated March 15, 2023. Accessed April 7, 2023. Available from https://www.uptodate.com/contents/treatment-of-metastatic-urothelial-cancer-of-the-bladder-and-urinary-tract?search=cisplatin%20ineligible&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.
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VIII. References (ENHANCED)

1e. Loriot Y, Necchi Am, Park SH, et al. Erdafitinib in Locally Advanced or Metastatic Urothelial Carcinoma. N Engl J Med 2019; 381:338-348.

2e. Yu EY, Pteryla 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 multicentre, single-arm, phase 2 trial. Lancet Oncol. 2021 Jun;22(6):872-882. doi: 10.1016/S1470-2045(21)00094-2.

3e. Powles T, Park SH, Voog E, et al. Maintenance avelumab + best supportive care (BSC) versus BSC alone after platinum-based first-line (1L) chemotherapy in advanced urothelial carcinoma (UC): JAVELIN Bladder 100 phase III interim analysis. J Clin Oncol. 2020;38(18_suppl):LBA1-LBA1.

4e. Hoimes C, Flaig T, Milowsky M, et al. Enfortumab vedotin plus pembrolizumab in previously untreated advanced urothelial cancer. J Clin Oncol 2023;41:22-31.

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6e. Prime Therapeutics Management. Padcev Clinical Literature Review Analysis. Last updated February 2025. Accessed February 2025.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C61	Malignant neoplasm of prostate
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C66.1	Malignant neoplasm of right ureter
C66.2	Malignant neoplasm of left ureter
C66.9	Malignant neoplasm of unspecified ureter
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified

ICD-10	ICD-10 Description
C68.0	Malignant neoplasm of urethra
D09.0	Carcinoma in situ of bladder
Z85.51	Personal history of malignant neoplasm of bladder
Z85.59	Personal history of malignant neoplasm of other urinary tract organ

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdictio	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC