Padcev™ (enfortumab vedotin-ejfv)
(Intravenous)

-E-

Document Number: MODA-0542

Last Review Date: 08/04/2020
Date of Origin: 06/02/2020
Dates Reviewed: 06/2020, 08/2020

I. Length of Authorization

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

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Padcev 20 mg single-dose vial: 15 vials of each 28-day cycle
- Padcev 30 mg single-dose vial: 15 vials of each 28-day cycle

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

- 500 billable units on days 1, 8 and 15 of every 28-day cycle

III. Initial Approval Criteria [1,2,3]

Coverage is provided in the following conditions:

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

Universal Criteria

- Used as a single agent; **AND**
- Patient does not have uncontrolled diabetes mellitus (i.e., baseline serum glucose > 250 mg/dL or hemoglobin A1C ≥ 8%); **AND**
- Patient does not have pre-existing peripheral neuropathy of Grade ≥ 2; **AND**
- Patient does not have active central nervous system (CNS) metastases; **AND**

Bladder Cancer/Urothelial Carcinoma † [4,9]

- Patient has one of the following diagnoses; **AND**
  - Locally advanced or metastatic urothelial carcinoma; **OR**
  - Local bladder cancer recurrence or persistent disease in a preserved bladder; **OR**
  - Local or metastatic bladder cancer recurrence post-cystectomy; **OR**
  - Recurrent or metastatic primary carcinoma of the urethra; **AND**
    - Patient does not have recurrence of stage T3-4 disease or palpable inguinal lymph nodes; **OR**

- Metastatic upper genitourinary (GU) tract tumors; **OR**
- Metastatic urothelial carcinoma of the prostate; **AND**

- Used as subsequent therapy; **AND**
- Patient experienced disease progression or recurrence after receiving treatment with the following:
  - Platinum-based therapy (i.e., carboplatin, cisplatin, etc.) in any treatment setting; **AND**
  - Immune checkpoint inhibitor therapy with a PD-directed agent (i.e., nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, 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 universal and indication specific criteria 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 peripheral neuropathy, ocular disorders including vision changes, severe skin reactions, etc.

V. Dosage/Administration

Indication	Dose
Bladder Cancer/Urothelial Carcinoma	Administer 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) administered as an intravenous infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- C9399 – Unclassified drugs or biologicals
- J9999 – Not otherwise classified, antineoplastic drugs
- J9177 – Injection, enfortumab vedotin-ejfv, 0.25 mg: 1 billable unit = 0.25 mg (Effective 7/1/2020)

NDC:

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

VII. References

1. Padcev [package insert]. Northbrook, IL; Astellas Pharma US, Inc; December 2019. Accessed July 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for enfortumab vedotin. National Comprehensive Cancer Network, 2020. 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 July 2020.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Bladder Cancer. Version 5.2020. National Comprehensive Cancer Network, 2020. 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 July 2020.
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.
7. Hematology/Oncology Pharmacy Association (2019). Intravenous Cancer Drug Waste Issue Brief. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
8. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
9. Loriot Y, Necchi Am, Park SH, et al. Erdafitinib in Locally Advanced or Metastatic Urothelial Carcinoma. N Engl J Med 2019; 381:338-348.
10. Magellan Health, Magellan Rx Management. Padcev Clinical Literature Review Analysis. Last updated July 2020. Accessed July 2020.

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
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)

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 Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs), Articles may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered 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		
Jurisdiction	**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)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate

Bladder Cancer/Urothelial Carcinoma

Subsequent Therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Enfortumab vedotin-ejfv	2A preferred	Yes	Phase 2 (EV-201), single-arm, multi-center	N/A	ORR	After PD-1/PD-L1 inhibitor and platinum-based therapy	• Enfortumab vedotin demonstrated a clinically meaningful response rate (ORR 44%) with a manageable and tolerable safety profile in patients with locally advanced or metastatic urothelial carcinoma who were previously treated with platinum and anti-PD-1/L1 therapies.
Erdafitinib	2A preferred	Yes for FGFR3 or FGFR2 genetic alterations	Phase 2 (BLC2001), open-label	N/A	ORR	After chemotherapy (unless ineligible to receive cisplatin)	• The use of erdafitinib was associated with an objective tumor response in 40% of previously treated patients who had locally advanced and unresectable or metastatic urothelial carcinoma with FGFR alterations. Treatment-related grade 3 or higher adverse events were reported in nearly half the patients.