

Drug Policy:

Padcev™ (enfortumab vedotin-ejfv)

POLICY NUMBER UM ONC_1381	SUBJECT Padcev™ (enfortumab vedotin-ejfv)		DEPT/PROGRAM UM Dept	PAGE 1 of 3
DATES COMMITTEE REVIEWED 02/12/20, 12/09/20, 08/11/21, 11/15/21, 05/11/22, 07/13/22, 05/10/23, 07/12/23, 10/11/23, 12/13/23	APPROVAL DATE December 13, 2023	EFFECTIVE DATE December 22, 2023	COMMITTEE APPROVAL DATES 02/12/20, 12/09/20, 08/11/21, 11/15/21, 05/11/22, 07/13/22, 05/10/23, 07/12/23, 10/11/23, 12/13/23	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Padcev (enfortumab vedotin-ejfv) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this NCH policy provided:

1. The requested medication was used within the last year, **AND**
2. The member has not experienced disease progression and/or no intolerance to the requested medication, **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Urothelial Cancer

1. Padcev (enfortumab vedotin-ejfv) may be used in combination with Keytruda (pembrolizumab) as first line therapy for locally advanced/metastatic urothelial carcinoma **ONLY** if the patient is ineligible to receive platinum-based chemotherapy (either using cisplatin or carboplatin)
 - a. Ineligibility for platinum-based therapy (using either cisplatin or carboplatin) is determined by the presence of **ONE** or more of the following:5 parameters:

- i. ECOG PS \geq 3,
 - ii. Cr Cl < 30 ml/min
 - iii. ECOG PS 2 AND Creatinine Clearance < 30 ml/minute
 - iv. Peripheral neuropathy \geq Grade 2: Moderate symptoms; limiting instrumental Activities of Daily Living
 - v. NYHA Heart Failure Class \geq 3: Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g., walking short distances (20-100m). Comfortable only at rest.
2. Above policy position is based on the updated survival of the JAVELIN Bladder 100 trial which showed equivalent overall survival (with carboplatin-based chemotherapy followed by avelumab maintenance) in patient with locally advanced/metastatic urothelial cancer, compared to the above regimen of Padcev + Keytruda. Ref: https://ascopubs.org/doi/abs/10.1200/JCO.2022.40.6_suppl.4.
 3. The member has locally advanced or metastatic urothelial carcinoma and Padcev (enfortumab vedotin-ejfv) is being used as a single agent in members who:
 - a. Have previously received Check Point Inhibitor therapy (e.g., pembrolizumab, avelumab, atezolizumab, nivolumab) and a platinum (cisplatin/carboplatin) containing chemotherapy regimen in the neoadjuvant/adjuvant, locally advanced, or metastatic setting **OR**
 - b. Have previously received Immune Checkpoint Inhibitor therapy (e.g., pembrolizumab, atezolizumab, nivolumab) and are ineligible for platinum-based therapy.

III. EXCLUSION CRITERIA

- A. Padcev (enfortumab vedotin-ejfv) is being used after disease progression with enfortumab containing regimen.
- B. Concurrent use with other chemotherapy and targeted therapies.
- C. Dosing exceeds single dose limit of Padcev (enfortumab vedotin-ejfv) 1.25 mg/kg (maximum 125 mg).
- D. Investigational use of Padcev (enfortumab vedotin-ejfv) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
 1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
 2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
 3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
 4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).

5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

- A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

- A. None

VII. REFERENCES

- A. Hoimes CJ, et al, EV-103/KEYNOTE-869 Clinical Trial. Enfortumab Vedotin Plus Pembrolizumab in Previously Untreated Advanced Urothelial Cancer. J Clin Oncol. 2023 Jan 1;41(1):22-31.
- B. Powles T, et al. EV-301 Clinical Trial. Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma. N Eng J Med 2021;384:1125—1135.
- C. Powles, et al. Avelumab First-Line Maintenance for Advanced Urothelial Carcinoma: Results From the JAVELIN Bladder 100 Trial After ≥2 Years of Follow-Up. Journal of Clinical Oncology 2023; 41: 3486-3492. DOI: <https://doi.org/10.1200/JCO.22.01792>
- D. Padcev prescribing information. Seattle Genetics, Inc. Bothell, WA 2022.
- E. Clinical Pharmacology Elsevier Gold Standard 2023.
- F. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.
- G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.
- H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.
- I. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.
- J. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.
- K. NCQA UM 2023 Standards and Elements.