CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Padcev Utilization Management Medical Policy
- Padcev® (enfortumab vedotin-ejfv intravenous infusion – Astellas and Seagen)

REVIEW DATE: 08/12/2026

OVERVIEW

Padcev, a Nectin-4-directed antibody and microtubule inhibitor conjugate, is indicated for the following:[1]

- **Bladder cancer** in adults:
  - As a single agent for the treatment of locally advanced or metastatic urothelial cancer in patients who:
    - Have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and platinum-containing chemotherapy.
    - Are ineligible for cisplatin-containing chemotherapy and have previously received ≥ one prior line of therapy.
  - In combination with Keytruda® (pembrolizumab intravenous infusion) or Keytruda Qlex® (pembrolizumab and berahyaluronidase alfa-pmph intravenous infusion) for the treatment of locally advanced or metastatic urothelial cancer.
  - In combination with Keytruda or Keytruda Qlex as neoadjuvant treatment and then continued after cystectomy as adjuvant treatment of muscle invasive bladder cancer (MIBC).

Guidelines

Padcev is addressed in National Comprehensive Cancer Network (NCCN) guidelines:

- **Bladder Cancer:** Guidelines (version 3.2026 – August 6, 2026) recommend Padcev for the subsequent treatment of locally advanced or metastatic urothelial carcinoma of the bladder, upper genitourinary tract, prostate, and urethra (category 2A).[3] In patients previously treated with both platinum-containing chemotherapy and a checkpoint inhibitor, but without prior enfortumab vedotin, Padcev monotherapy is a preferred option (category 1). Padcev monotherapy is also recommended (category 2A) after prior platinum-containing chemotherapy alone (as an "other recommended" option) or as a preferred option prior to checkpoint inhibitor alone, in patients without prior enfortumab vedotin. In addition, NCCN recommends Padcev, in combination with Keytruda, for the preferred first-line treatment (category 1) and as a second-line option (category 2A) after chemotherapy, immunotherapy, or both – preferred after prior chemotherapy alone, preferred after prior immunotherapy alone, and "other recommended" after both prior chemotherapy and immunotherapy – for locally advanced or metastatic urothelial carcinoma of the bladder, upper genitourinary tract, prostate, and urethra. NCCN also recommends perioperative/sandwich therapy Padcev plus Keytruda as a preferred regimen for MIBC (category 2A), regardless of cisplatin eligibility.
- **Head and Neck Cancers:** Guidelines (2.2026 – May 12, 2026) recommend Padcev as a single agent that is useful in certain circumstances for recurrent, unresectable, or metastatic non-nasopharyngeal head and neck cancer with no surgical or radiotherapy option, in patients with disease progression on or after platinum therapy and a PD-1/PD-L1 inhibitor (category 2B).[4]

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POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Padcev. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Padcev as well as the monitoring required for adverse events and long-term efficacy, approval requires Padcev to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Padcev is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Bladder Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has muscle invasive bladder cancer and meets BOTH of the following (a and b):
       - **a)** The medication is used in combination with Keytruda (pembrolizumab intravenous infusion) or Keytruda Qlex (pembrolizumab and berahyaluronidase alfa-pmph intravenous infusion); AND
       - **b)** The medication is used as neoadjuvant or adjuvant therapy; OR
     - **ii.** Patient has locally advanced or metastatic disease and meets ONE of the following (a or b):
       - **a)** The medication is used as first-line in combination with Keytruda (pembrolizumab intravenous infusion) or Keytruda Qlex® (pembrolizumab and berahyaluronidase alfa-pmph intravenous infusion); OR
       - **b)** The medication is used as subsequent therapy; AND
   - **C)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve ONE of the following dosing regimens (A or B):
   - **A)** Approve up to 125 mg administered intravenously no more frequently than three times in each 28-day cycle; OR
   - **B)** Approve up to 125 mg administered intravenously no more frequently than twice in each 21-day cycle.

Other Uses with Supportive Evidence

2. **Head and Neck Cancers.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has non-nasopharyngeal disease; AND
     Note: Examples of non-nasopharyngeal disease include: oral cavity, oropharynx, hypopharynx, glottic larynx, supraglottic larynx, ethmoid and maxillary sinus, and occult primary.

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C) Patient has progressed on or after platinum therapy and a programmed death receptor 1 (PD-1)/ programmed death-ligand 1 (PD-L1) inhibitor; AND
Note: Examples of platinum therapy include carboplatin and cisplatin. Examples of PD-1/PD-L1 inhibitors include Keytruda (pembrolizumab intravenous infusion), Keytruda Qlex (pembrolizumab and berahyaluronidase alfa-pmph subcutaneous injection), Opdivo (nivolumab intravenous infusion), and Opdivo Qvantig (nivolumab and hyaluronidase-nvhy subcutaneous injection).

D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 125 mg administered intravenously no more frequently than three times in each 28-day cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Padcev is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Padcev® intravenous infusion [prescribing information]. Northbrook, IL: Astellas Pharma; November 2025.
2. The NCCN Bladder Cancer Clinical Practice Guidelines in Oncology (version 3.2026 – August 6, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 6, 2026.
3. The NCCN Drugs and Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 6, 2026. Search term: enfortumab.
4. The NCCN Head and Neck Cancer Clinical Practice Guidelines in Oncology (version 2.2026 – May 12, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 6, 2026.
5. Swiecicki PL, Yilmaz E, Rosenberg AJ, et al. Phase II Trial of Enfortumab Vedotin in Patients With Previously Treated Advanced Head and Neck Cancer. *J Clin Oncol*. 2025;43(5):578-588.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	01/29/2025
Annual Revision	**Urothelial Carcinoma:** The requirement that Padcev is used in combination with Keytruda (pembrolizumab intravenous infusion) was modified to Padcev is used in combination with Keytruda (pembrolizumab intravenous infusion) or Keytruda Qlex® (pembrolizumab and berahyaluronidase alfa-pmph intravenous infusion).	01/07/2026
Early Annual Revision	**Bladder Cancer:** Indication was changed to as listed. Previously listed as Urothelial Carcinoma. The patient has muscle invasive bladder cancer AND the medication is used in combination with Keytruda (pembrolizumab intravenous infusion) or Keytruda Qlex (pembrolizumab and berahyaluronidase alfa-pmph intravenous infusion) as neoadjuvant or adjuvant therapy was added as an option for approval. **Head and Neck Cancers.** This was added as a new condition of approval under "Other Uses with Supportive Evidence."	08/12/2026

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