

Clinical Policy: Enfortumab Vedotin-ejfv (Padcev)

Reference Number: LA.PHAR.455

Effective Date: 10.25.23

Last Review Date: ~~02.23.26~~03.04.25

Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

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See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description

Enfortumab vedotin-ejfv (Padcev[®]) is a Nectin-4-directed antibody and microtubule inhibitor conjugate.

FDA Approved Indication(s)

Padcev is indicated:

- 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 ~~locally advanced or metastatic urothelial~~ muscle invasive bladder cancer (MIBC) who are ineligible for cisplatin-containing chemotherapy
- In combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC)
- As a single agent for the treatment of adult patients with locally advanced or ~~metastatic urothelial cancer mUC~~ 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
 - are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections[®] that Padcev is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. ~~Urothelial Carcinoma~~ **Bladder Cancer** (must meet all):

1. Diagnosis of ~~recurrent, locally advanced, or metastatic (stage IV)~~ urothelial carcinoma or MIBC;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. ~~One~~For MIBC: Both of the following (a and b):
 - a. Prescribed in one of the following ways (i or ii):

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i. Neoadjuvant treatment in combination with Keytruda® or Keytruda Qlex™ for up to 3 cycles;

ii. Adjuvant treatment in combination Keytruda or Keytruda Qlex following neoadjuvant treatment and cystectomy for up to 6 cycles;

b. Member is ineligible for cisplatin-containing chemotherapy;

4-5. For recurrent, locally advanced, or metastatic urothelial carcinoma, one of the following (a or b):

a. Prescribed as a single agent, and one of the following (i or ii):

i. Failure of both of the following (1 and 2):

- 1) Platinum-containing chemotherapy (*see Appendix B*);
- 2) PD-1 or PD-L1 inhibitor (*see Appendix B*);

ii. Member is ineligible for cisplatin-containing chemotherapy and has previously received one or more prior lines of therapy (*see Appendix B*);

b. Prescribed in combination with Keytruda® or Keytruda Qlex;

5-6. Request meets one of the following (a, b, or c):*

a. ~~If~~ For urothelial carcinoma if prescribed as a single agent: Dose does not exceed 1.25 mg/kg (up to 125 mg) on days 1, 8, and 15 of a 28-day cycle;

b. If prescribed in combination with Keytruda or Keytruda Qlex: Dose does not exceed 1.25 mg/kg (up to 125 mg) on days 1 and 8 of a 21-day cycle;

c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6-12 months.

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B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53.

II. Continued Therapy

A. ~~Urothelial Carcinoma~~ **Bladder Cancer** (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Padcev for a covered indication and has received this medication for at least 28 days;
2. Member is responding positively to therapy;
3. If request is for MIBC, maximum duration of therapy does not exceed both of the following (a and b):
 - a. For neoadjuvant treatment: 3 cycles;
 - b. For adjuvant treatment: 6 cycles;

3-4. If request is for a dose increase, request meets one of the following (a, b, or c):*

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- a. ~~If~~ **For urothelial carcinoma if** prescribed as a single agent: New dose does not exceed 1.25 mg/kg (up to 125 mg) on days 1, 8 and 15 of a 28-day cycle;
- b. If prescribed in combination with Keytruda **or Keytruda Qlex**: New dose does not exceed 1.25 mg/kg (up to 125 mg) on days 1 and 8 of a 21-day cycle;
- c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

- 1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
- 2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy ~~yes~~ LA.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

PD-1: programmed death receptor-1

PD-L1: programmed death-ligand

MIBC: muscle invasive bladder cancer

mUC: metastatic urothelial cancer

NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of platinum-containing regimens		
DDMVAC (dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin)	Varies	Varies
gemcitabine with either cisplatin or carboplatin	Varies	Varies
Examples of PD-1 inhibitors		
Keytruda® (pembrolizumab)	Varies	Varies

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<u>Keytruda Qlex™ (pembrolizumab and berahyaluronidase alfa-pmp)</u>	<u>Varies</u>	<u>Varies</u>
Opdivo® (nivolumab)	Varies	Varies
<u>Opdivo Qvantig™ (nivolumab and hyaluronidase-nvhy)</u>	<u>Varies</u>	<u>Varies</u>
Examples of PD-L1 inhibitors		
Tecentriq® (atezolizumab)	Varies	Varies
Imfinzi® (durvalumab)	10 mg/kg IV infusion every 2 weeks	Varies
Bavencio® (avelumab)	800 mg IV infusion once every 2 weeks	Varies
Other recommended regimens		
gemcitabine	Varies	Varies
gemcitabine and paclitaxel	Varies	Varies
ifosfamide, doxorubicin, gemcitabine	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): serious skin reactions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
<u>MIBC</u>	<u>1.25 mg/kg (up to a maximum dose of 125 mg) given as an IV infusion over 30 minutes as neoadjuvant treatment on Days 1 and 8 of each 21-day cycle for 3 cycles or until disease progression that precludes curative intent cystectomy or unacceptable toxicity, followed by adjuvant treatment on Days 1 and 8 of each 21-day cycle for 6 cycles or until disease recurrence or unacceptable toxicity</u>	<u>1.25 mg/kg (up to a maximum dose of 125 mg)</u>
Urothelial cancer	<p>As a single agent: 1.25 mg/kg (up to a maximum dose of 125 mg) given as an IV infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity</p> <p>In combination with Keytruda: 1.25 mg/kg (up to a maximum dose of 125 mg) given as an IV infusion over 30 minutes on Days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity</p>	See dosing regimen 1.25 mg/kg (up to a maximum dose of 125 mg)

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VI. Product Availability

Single-dose vial for injection: 20 mg, 30 mg

VII. References

1. Padcev Prescribing Information. Northbrook, IL: Astellas Pharma US, Inc; ~~August 2024~~November 2025. Available at: <https://www.padcev.com>. Accessed ~~October 21, 2024~~November 25, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November ~~7, 2024~~19, 2025.
3. National Comprehensive Cancer Network. Bladder Cancer Version ~~5.2024~~2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed November ~~7, 2024~~19, 2025.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November ~~7, 2024~~19, 2025.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9177	Injection, enfortumab vedotin-ejfv, 0.25 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created.	05.01.23	09.25.23
Annual review: for urothelial cancer in combination with Keytruda, updated FDA-approved indication to full approval and removed requirement for cisplatin ineligibility per updated PI.	05.01.24	07.29.24
Annual review: no significant changes; references reviewed and updated.	03.04.25	<u>05.19.25</u>
<u>Annual review: extended initial approval duration from 6 to 12 months for this maintenance medication for a chronic condition; added option to be prescribed in combination with Keytruda Qlex; references reviewed and updated; new indication for MIBC added per updated prescribing information.</u>	<u>02.23.26</u>	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

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approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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